At the conclusion of this exercise, the student will be able to counsel patients regarding potential consequences of the following conditions in pregnancy:

A. Anemia
B. Diabetes mellitus
C. Urinary tract disorders
D. Infectious diseases, including
   1. Herpes
   2. Rubella
   3. Group B Streptococcus
   4. Hepatitis
   5. Human Immunodeficiency virus (HIV), human papillomavirus (HPV), and other sexually transmitted infections
   6. Cytomegalovirus (CMV)
   7. Toxoplasmosis
   8. Varicella and parvovirus
E. Cardiac disease
F. Asthma
G. Surgical abdomen
I. Anemia

A. Hematological adaptation to pregnancy
   - Expanded blood volume
   - Increased red cell volume
   - Increased plasma volume

B. Normal values during pregnancy
   - Hemoglobin/hematocrit (10-14 gm/dL; 35-45 vol%)
   - Increased procoagulants – fibrinogen, factors VII, VIII, IX, X

C. Anemia’s
   - Clinical symptoms
     - Easy fatigue
     - Lethargy
     - Headaches
     - Pica
     - Shortness of breath
     - Palpitations
     - Dizziness
   - Clinical exam
     - Pallor
     - Splenomegaly
   - Types of anemia
     - Nutritional deficiencies
       - Iron
         - Incidence – 75% of all anemia’s
         - Clinical – glossitis, cheilitis
         - Laboratory findings
           - Hypochromic
           - Microcytic
           - Schistocytes
           - MCV decreased
           - Serum iron decreased
           - Transferrin saturation decreased
         - Differential diagnosis
           - Inflammatory process
           - Chemical toxicity
           - Malignancy
           - Hemoglobinopathies
       - Vitamin deficiencies
- Megaloblastic anemia
  - Folic acid or B₁₂ deficiency, or compliant AZT usage
  - Due to impaired DNA synthesis
  - Second most common type of anemia
  - Mechanism
    - B₁₂ slows conversion of ribonucleotide to deoxynucleotides
    - Folate deficiency precludes appropriate DNA synthesis
  - Laboratory
    - Hypersegmented granulocytes
    - RBC inclusions
      - Howell Jolly bodies
      - Basophilic stippling
    - Normochromic
    - Macrocytic (MCV > 100)
    - Increased serum iron
    - Increased transferrin
    - Fasting folate < 3 µ/L
    - Schilling test (non-pregnant)
    - B₁₂ RIA < 50 pg/ml
  - Therapy
    - Folic acid – 0.5 mg TID orally
    - B₁₂ – 1 mg/wk

D. Hemoglobinopathies

- Sickle cell disease (Hb SS)
  - Frequency 1:708
  - 1:625 at birth
  - 1:1875 at reproduction
  - Etiology – valine replaces glutamic acid at position 6 in β-chain; therefore, patients have no HbA
  - Clinical
    - Retarded growth and development
    - Skeletal changes
    - Decreased life span
    - Sickle cell crisis
    - Hyperdynamic circulation
    - Cardiomegaly
    - Heart failure
    - Pneumonia
    - Vascular occlusion
    - Hepatomegaly
    - Splenic infarction
- Bone marrow infarction
- Osteomyelitis
- Arthritis
- Convulsions

· Laboratory
  - Increased serum iron
  - Folate deficiency
  - Hemoglobin electrophoresis

· Pregnancy consequences
  - Spontaneous abortion not increased
  - Perinatal mortality (before 1979) increased
  - Low birth weight (before 1979) increased

· Management during pregnancy
  - Supportive therapy
  - Transfusions
  - Partial exchange transfusion
    - Hct > 35% or
    - Hb A level > 40%
  - Prophylactic transfusions – maintain % S ≤ 50%

• Thalassemia
  · Worldwide distribution
  · Types
    - β-thalassemia major (Cooley's anemia)
      - Little or no production of β-chains
      - Abnormal cells with Heinz bodies and nucleated red cells
    - β-thalassemia minor
      - High red cell count
      - Microcytosis
      - Microcytic hypochromatic erythrocytes
      - Hemoglobin A₂ > 3.5%
    - α-thalassemia
      - Homozygous-all 4 genes deleted-no α-globin chains produced
      - HbH – 3 α-globin genes deleted
      - α-thalassemia-1 – 2 genes deleted

E. Coagulopathies – specifically associated with pregnancy

• Placental abruption
  · Symptoms – pain, ± bleeding, shock
  · Lab findings
    - Hypofibrinogenemia
    - Increased fibrin-split products
    - Renal insufficiency
• Mechanism – intravascular and retroplacental coagulation with subsequent activation of plasminogen to plasmin

• Management
  - Blood replacement
  - Prompt delivery
  - ± factor replacement

• Amniotic fluid embolus (AFE)—also called “Anaphylactoid Syndrome of Pregnancy”
  • Symptoms – sudden respiratory distress and circulatory collapse followed by DIC
  • Lab findings – hypoxia, thrombocytopenia
  • Mechanism
    - Particulate-matter induced pulmonary artery obstruction
    - Decreased intravascular fibrinogen
    - Increased fibrin-split products
    - DIC
  • Management – intense respiratory support; Swan Ganz monitoring ± blood component therapy

• Fetal death
  • Incidence of coagulopathy – 25% if fetus is dead > 4 wk.
  • Lab findings – gradual decrease in fibrinogen, some increase in fibrin-split products and thrombocytopenia
  • Pathogenesis – thromboplastin from dead fetus
  • Management
    - Heparin to correct coagulation defect
    - After correction → delivery

• Acute fatty liver
  • Pathogenesis – increased consumption of procoagulants and impaired production
  • Symptoms – anorexia, malaise, vomiting, nausea, upper abdominal pain, progressive jaundice
  • Lab findings
    - Hypofibrinogenemia
    - Elevated serum fibrin-split products
    - ± thrombocytopenia
    - Elevated serum ammonia
  • Management – delivery, blood, blood component therapy

• Preeclampsia-eclampsia
  • Significance of coagulopathy
    - Bleeding
    - Ischemic tissue damage
    - Microangiopathic hemolysis
      - Anemia
- Hemoglobinemia
- Hemoglobinuria
- Erythrocyte abnormalities
- Laboratory evidence of defective hemostasis
  - Hypofibrinogenemia
  - Thrombocytopenia
  - Prolonged PT and PTT
  - Prolonged thrombin time
- Management – delivery

II. Diabetes mellitus
A. Incidence
  - 0.2 to 0.3% of pregnancies with preconceptional diabetes
  - 3-12% of pregnancies with gestational diabetes
B. Classification

<table>
<thead>
<tr>
<th>Class</th>
<th>Onset Age (Yr.)</th>
<th>Duration (Yr.)</th>
<th>Vascular Disease</th>
<th>Insulin Need</th>
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<td>0</td>
<td>0</td>
</tr>
<tr>
<td>A2</td>
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<td>+</td>
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<tr>
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<td>&lt;10</td>
<td>0</td>
<td>+</td>
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<td>Any</td>
<td>Any</td>
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</tr>
</tbody>
</table>


C. Diagnosis – screening
  - Universal Screening recommended
• If not, do screens based on risk factors – high-risk if
  • > 25 y/o
  • Primary relative with DM
  • Previous macrosomic infant (≥ 4,000 gm)
  • Previous malformed or stillborn infant
  • Obesity (≥50% ideal body weight)
  • Glycosuria

• Method
  • 50 gm glucola between wk. 24 and 28; plasma value > 140 mg/dL cutoff
  • If positive; 100 gm glucola (see normal values below)

<table>
<thead>
<tr>
<th>DETECTION OF GESTATIONAL DIABETES</th>
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</thead>
<tbody>
<tr>
<td><strong>Plasma Level</strong></td>
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<tr>
<td>(mg/dL)</td>
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<tr>
<td>(mmol/L)</td>
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<tr>
<td><strong>Screening test – 50 g</strong></td>
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<tr>
<td>1 hr</td>
</tr>
<tr>
<td>&lt; 140</td>
</tr>
<tr>
<td>7.8</td>
</tr>
<tr>
<td><strong>Diagnostic test – 100 g oral glucose tolerance</strong></td>
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<tr>
<td>Fasting</td>
</tr>
<tr>
<td>&lt; 105</td>
</tr>
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<td>5.8</td>
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<tr>
<td>2 hr</td>
</tr>
<tr>
<td>&lt; 165</td>
</tr>
<tr>
<td>9.2</td>
</tr>
<tr>
<td>3 hr</td>
</tr>
<tr>
<td>&lt; 145</td>
</tr>
<tr>
<td>8.0</td>
</tr>
</tbody>
</table>

* Diagnosis of gestational diabetes is made when any two values are met or exceeded.

D. Effect of pregnancy on diabetic patient (end-organ)
• Retinopathy
  • Classification
    - Background diabetic retinopathy (BDR) – non-proliferative (less severe)
    - Proliferative diabetes retinopathy (PDR) – (signals worsening)
  • Risk factors – not well-defined
    - Age of onset and duration of diabetes important
    - 2% of patients with diabetes < 5 yr.
    - 15.5% with diabetes > 15 yr.
  • Treatment
    - Good vision, BDR, macular edema – photocoagulation helpful
    - PDR – panretinal photocoagulation does reduce risk of severe visual loss
Treatment should be instituted during pregnancy if needed.

Pregnancy – retinopathy may worsen because of:
- Tight control associated with pregnancy
- Natural history of disease
  - Subsequent pregnancies – no relationship between worsening of disease and number of subsequent pregnancies

Suggestions
- Initiate good control of glucose prior to pregnancy to avoid worsening retinopathy with onset of good control in pregnancy
- Photocoagulate lesions prior to pregnancy

Nephropathy
- Stages
  - Early hypertrophy – hyperfunction
  - Glomerular lesions without clinical disease
  - Microalbuminuria
  - Macroalbuminuria
  - End stage renal disease
- Associated with
  - Hypertension (avoid thiazides and β-Blockers for treatment. Suggest using Aldomet, hydralazine, prazosin, calcium channel blockers)
  - Anemia in 42% – caused by decrease in erythropoietin
  - Retinopathy
- Course during pregnancy
  - If proteinuria present, usually increases during pregnancy; usually subsides after pregnancy.
  - Usual increase in creatinine clearance does not occur (depending on severity of nephropathy)
  - 30% will have diminution of renal function during pregnancy; usually subsides after pregnancy
  - Overall subsequent decline not hastened by pregnancy

Neuropathy

Coronary artery disease
- Class H, arteriosclerotic heart disease
  - 2/3 to 3/4 patients die in peripartum period.
  - If angina or MI history discourage pregnancy or advise termination.
  - These patients have less than normal increase in left ventricular size and stroke volume.

E. Effect of diabetes on pregnancy
- Maternal system
- PIH overall incidence 11.7%
  - DFR incidence is definitely increased
- Chronic hypertension
  - Incidence 9.6%
  - Gestational diabetes; B, C, similar to general population
  - Class D → F significantly increase incidence
- Ketoacidosis (9.3% incidence) (DKA)
  - More common in diabetics > 5 yr. or illness (flu or infection)
  - DKA can occur in gestational diabetes treated with β-agonists for preterm labor
- Pyelonephritis (4.3%)
  - Associated with increased perinatal mortality
  - Increased incidence in class C-R
- Hydramnios (15.7% overall incidence)
  - Same frequency in class B-R
  - 85% of diabetic subjects no other etiology than maternal disease
- Preterm labor
- Cesarean delivery
  - Primary rate increases with gestational diabetes → C, further increased D-R
  - Due to failed induction, macrosomia, fetal distress
- Maternal mortality
  - 10-fold increase over that of non-diabetics
  - Before insulin 6-50% risk of mortality
  - With current management, risk is 0.11 to 0.5%
  - Reason – cardiac arrest, DKA, sepsis, hypoglycemia, hemorrhage
- Fetal system (perinatal mortality 2-5%)
- Congenital malformation
  - Major anomalies 6-13%
  - Accounts for 40% of perinatal deaths
  - Probably not an increase in gestational diabetes
  - Anomalies include:
    - Craniospinal defects (NTD)
      - 19.5/1000 (reduction in cell mitosis and premature specialization)
      - Caudal regression 0.2 to 0.5%
    - Microcephaly
    - Cardiac 4% – more commonly aortic anomalies or ventricular septal defect
    - Renal – agenesis, duplication, hydronephrosis
    - G.I.-T-E fistula, duodenal atresia, anorectal
atresia, imperforate anus
- Single umbilical artery – 6.4%
- Specific congenital malformations in infants of diabetic mothers
  - Cardiovascular
    - Transposition of the great vessels
    - Ventricular septal defect
    - Atrial septal defect
    - Hypoplastic left ventricle
    - Situs inversus
    - Aortic anomalies
  - Central nervous system
    - Anencephaly
    - Encephalocele
    - Meningomyelocele
    - Microcephaly
  - Skeleton
    - Caudal regression syndrome
    - Spina bifida
  - Genitourinary
    - Absent kidneys (Potter's syndrome)
    - Polycystic kidneys
    - Double ureter
  - Gastrointestinal
    - Tracheoesophageal fistula
    - Bowel atresia
    - Imperforate anus

Etiology of anomalies (occurs before 7 wk. gestation)
- Metabolic factors
- High glucose level associated but not cause per se
- Hypoglycemia not cause
- Insulin doesn't cross placenta
- Strict control will decrease anomalies
- Class D-F increased incidence, (hypoxia due to vascular disease)?
- Target for malformation is yolk sac

F. Management
- Preconceptional – counseling
  - Assess health in regard to end organ damage
  - Plan pregnancy
  - Obtain optimal diabetic control
  - Check rubella status
  - Folate 0.4 mg qd
- Antenatal management
- Gestational diabetes
  - Diet, 35 Kcal/kg (IBW)
  - FBS and 2 hr p.p. every 2 wk.
  - If hyperglycemic – add insulin (highly purified) (Gabbe suggest > 120 on 2 or more occasions within 2-wk interval)
- Insulin dependent
  - Diet 35-38 Kcal/kg ideal body weight (20% protein, 35% fat, 45% carbohydrates)
  - Metabolic control (discontinue oral hypoglycemics)
    - Insulin
      - Administration
        - Subcutaneous route – 2 injections/day
          - 2/3 dose am 2:1 NPH/regular
          - 1/3 dose PM 1:1 NPH/regular
        - Subcutaneous route—injections at meals and hs
        - Subcutaneous route—carb counting, long-acting insulin
        - Subcutaneous route—insulin pump
  - Maternal home glucose monitoring
    - Glucose oxidase impregnated reagent strips.
      - (Normal pregnancy range 70-130 mg/dL, goals vary in literature; value between 90-150 mg/dL seems appropriate.)
  - Fetal monitoring
    - Prenatal diagnosis
      - Glycosylated hemoglobin
        - > 12% – increased risk as high as 22.4% congenital anomalies
      - MSAFP
    - Sonography – level II scan at 18-20 wk.; fetal echocardiography if available particularly if HgbA1C is > 8.5%
      - ACOG Bulletin recommends NST weekly after 30 wk.; if nonreactive, proceed with OCT
        - NST – test fetal state
        - OCT – test fetal reserve
    - Biophysical profile – time consuming, requires specifically trained personnel
    - Maternal education – fetal movement < 10 in 12 hr may be associated with fetal compromise
• Delivery
  • Timing – individualized – per ACOG
    - If health of mother and fetus appear well – delay delivery until term and await spontaneous labor.
    - If patient develops complications, decision is based on degree of risk vs. fetal maturity
  • Mode
    - Diabetes in itself not reason for cesarean delivery
    - Cesarean delivery based on obstetrical reasons
    - EFW > 4000 you may consider primary cesarean delivery without labor or if history of shoulder dystocia present
    - Avoid mid-forceps
  • Management
    - Maintain euglycemia (IV insulin during labor)
    - Observe for neonatal hypoglycemia
• Postpartum
  • Insulin requirements
    - Requirements decrease due to decrease in estrogen and placental lactogen – sensitivity to insulin increases
    - May not require insulin for 48-96 hr.; must be aware of potential for hypoglycemia
  • Counseling
    - If gestational diabetic – repeat glucose tolerance test at 6-12 wk. (75 gm load) postpartum
    - Make patient aware of increased incidence of developing overt diabetes (60% in 16 yr.)
    - Subsequent pregnancy recurrence of gestational diabetic in about 60%
  • Contraception
    - Oral contraceptive pills (OCP)
    - May require increase of insulin (8-20u)
    - Intrauterine device (not recommended)
      - Risk of infection at insertion and if exposed to STD
    - Barrier method – acceptable, if used
    - Progestogen-only O.C.
      - If taken regularly, small failure rate
      - Norethindrone – no change in lipids or clotting factors
    - Depo-Provera
    - Natural family planning – motivation required
    - Sterilization – tubal ligation vs. vasectomy

III. Urinary tract infections (UTI)
A. Asymptomatic bacteriuria in pregnancy

- **Definition**
  - Persistent, actively-multiplying bacteria within urinary tract
  - > 10^5 bacteria/ml collected on 2 clean catch midstream urines of a single uropathogen

- **Prevalence**
  - 2-11%
  - 7-8% (at Parkland Memorial Hospital)

- **Risk Factors**
  - Lower socioeconomic class
  - Sickle cell trait and sickle cell anemia
  - Reduced availability of medical care
  - Increased parity
  - Older age

- **Pathophysiology**
  - Short urethra
  - Physiologic changes of pregnancy
    - Increased pH
    - Aminoaciduria
    - Ureteral dilatation
    - Bladder hypotonia
  - Other factors
    - Mechanical compression of ureter
    - Inhibitory effect of progesterone on ureteral smooth muscle
    - Enhanced growth of coliform bacteria

- **Pathogens**
  - *E. coli* – 75%
  - *P. mirabilis* – 8%
  - *K. pneumoniae* – 20%
  - *Staph saprophyticus* 15-20%
  - *S. fecalis* – < 5%
  - *S. agalactiae*

- **Pathways**
  - Ascending infection
  - Contamination/colonization from perineum

- **Clinical findings**
  - Asymptomatic
  - Urinalysis – few WBC, bacteria positive
  - 50% have asymptomatic bacteriuria of renal origin

- **Adverse effects**
  - Pyelonephritis if untreated
  - Controversial
    - Low birth weight
- Anemia
- Pregnancy-induced hypertension

- **Treatment**
  - Initial infection
    - Nitrofurantoin 100 mg qhs for 10 days
    - Nitrofurantoin 100 mg BID x 3 days
  - Recurrent disease – Macrodantin 100 mg every 6 hr. x 10 days
  - Alternative medications
    - Trimethoprim-sulfamethoxazole DS po BID 7 days
    - Gantresin (sulfisoxazole) 500 mg q6 hr. x 3-7 days

**B. Acute urethritis**

- **Incidence** – unknown
- **Risk factors**
  - Trauma
  - Sexual encounters
- **Microbiology**
  - Coliform organisms, i.e. *E. coli*
  - *N. gonorrhoeae*
  - *C. trachomatis*
- **Clinical findings**
  - Dysuria
  - Frequency
  - Urgency
  - Hesitancy
  - Urethral discharge (purulent)
- **Diagnosis**
  - Urinalysis
    - Leukocytes
    - Bacteria ±
    - No WBC casts
    - Red cell casts ±
  - Urine culture – may be negative
  - Urethral culture – may be positive for *N. gonorrhoeae* or *C. trachomatis*
- **Treatment**
  - Coliform – oral antibiotics and cost
    - Sulfonamides – low
    - SMX-TMP – moderate
    - Ampicillin – low
    - Augmentin – high
    - Cephalosporin – low
    - Nitrofurantoin – moderate
  - *N. gonorrhoeae*
    - Ceftriaxone 250 mg IM x 1
- Cefuroxime axetil 1 gm po
  PLUS
- Probenecid 1 gm po
- Cefixime 400 mg po x 1
- Spectinomycin 2 gm IM x 1

C. trachomatis
- Erythromycin 500 mg po qid x 7 days
- Azithromycin 1 gm po
- Ampicillin 500 mg po TID x 7 days

C. **Acute cystitis**

- **Definition**
  - Infection limited to lower urinary tract
  - Local symptoms
  - No systemic symptoms
  - > 100 bacteria/ml of single uropathogen

- **Etiology** – arises denovo
- **Pathogenesis** – ascending infection from minor urethral trauma
- **Prevalence**
  - 1-2% of all pregnancies
  - Not usually preceded by asymptomatic bacteriuria

- **Clinical findings**
  - Lower tract irritative symptoms – dysuria, frequency, urgency, hesitancy, dribbling, hematuria
  - Suprapubic discomfort

- **Diagnosis**
  - Urinalysis – WBCs, bacteria, red cells
  - Urine culture – single uropathogen
  - Urine nitrates
    - Low sensitivity
    - High specificity
  - Leukocyte esterase
    - Low sensitivity
    - High specificity
  - Nitrates plus leukocyte esterase > 90% sensitivity and specificity

- **Treatment**
  - Nitrofurantoin 100 mg x 4/day for 7-10 days
  - OR
  - Nitrofurantoin macrocrystals
  - Gantrinsin 500 mg x 5/day for 3-7 days
  - Cephalosporins i.e. Keflex, 250 mg x 4/day for 3-7 days
  - Ampicillin 250 mg x 4/day for 3-7 days

D. **Pyelonephritis**

- **Incidence/occurrence**
  - First trimester – 9%
• Second trimester – 41%
• Third trimester – 50%

- Presenting symptoms
  - Back pain and chills – 82%
  - Lower tract irritative symptoms – 40%
  - Nausea/vomiting – 24%

- Clinical findings
  - Temperature > 38° – 84%
  - Temperature > 40° – 12%
  - Right CVAT – 54%
  - Bilateral CVAT – 27%
  - Left CVAT – 16%

- Pathogens
  - *E. coli* – 72-75%
  - *Klebsiella-enterobacter* – 23%
  - *Proteus* – 4%

- Multisystem derangement
  - Hypothalamic instability – wide temperature swings
  - Respiratory insufficiency – 2% of pregnant women with pyelonephritis
    - Clinical ARDS
      - Tachypnea
      - Hypoxia
    - Treatment
      - Oxygen 100% via face mask
      - Lasix 20 mg IV
      - +\- Mechanical ventilation
        - If respiratory rate > 35
        - If PaO₂ < 70 mmHg
        - If PaCO₂ > 55 mmHg
  - Renal dysfunction
    - Seen in 25%
    - Transient
    - Creatinine ≥ 0.8 mg/dL – CrCl < 80 cc/min
  - Anemia
    - Seen in 25%
    - Transient
    - Etiology – LPS (bacterial endotoxin) effects on erythrocyte
      - No alteration in erythropoietin
  - Cardiac
    - Total peripheral resistance decreased
    - Cardiac output increased

- Failed therapy
• Perinephric abscess
• Perinephric phlegmon (lobar nephronia)
• Septicemia/shock

• Treatment
  • Hospitalization vs outpatient
  • Aggressive hydration
  • Empiric therapy
    - Ampicillin/gentamicin
    - Ureidopenicillins
    - Cephalosporins
    - Ceftriaxone

• Fetal considerations – preterm labor
  • 85% have contractions within 1 hr. after therapy
  • 50% have persistent contractions after 5 hr.

IV. Herpes simplex virus (HSV)
A. Virology
  • Types
    • HSV-1 – predominantly oral (although 15% of genital infection is due to HSV-1)
    • HSV-2 – predominantly genital
  • Linear double stranded DNA core surrounded by glycoprotein envelope
  • Latent infection

B. Incidence
  • STD clinic – 48%
  • Estimated total cumulative – 20 million

C. Epidemiology
  • Endemic in USA
  • ~ 750,000 new cases/yr.
  • Incidence 1-2% of population
  • Antibody titers
    • HSV-1 at age 30 – lower socioeconomic – 80%
    • HSV-2
      - Caucasians – 20%
      - African Americans – 40-60%
  • Cumulative prevalence > 20 million affected
  • Risk factors
    • Older
    • Educated
    • Married
    • Caucasians

D. Pathogenesis
  • Sexual transmission
  • Oral/genital contact
• Perinatal transmission
• Aerosol and fomite spread – unusual since virus inactivated at room temperature

E. Incubation period – 2-12 days (mean 6 days)

F. Clinical findings
• Three distinct types
  • First episode primary – no circulating HSV-1 or HSV-2 antibodies
  • First episode non-primary – with circulating antibodies (to either HSV-1 [most patients] or HSV-2)
  • Recurrent disease
• Primary
  • Occurring in individuals for first time – no serologic evidence of previous infection
  • Systemic symptoms (more common in women)
    - Fever
    - Malaise
    - Myalgia
    - Headache
  • Local symptoms
    - Pain
    - Itching
    - Dysuria
    - Vaginal discharge
    - Tender inguinal adenopathy
  • Duration of lesions
    - HSV-2 – 18.6 days
    - HSV-1 – 22.7 days
    - Nonprimary HSV-2 – 15.5 days
  • Duration of viral shedding – 11-12 days
  • Cervical shedding common (80-86%)

• Recurrent
  • Reactivation or reinfection of previous infection
  • Milder, self-limited
  • Localized
  • Usually lasts 6-7 days
  • Duration of viral shedding – 45 days
  • Prodrome – 1-2 days
  • Cervical lesions uncommon

G. Diagnosis
• Clinical diagnosis most common
• Virus isolation – most sensitive
  • Gold standard
  • 5-20% false negative rate due to other viral infections, i.e. CMV
Grows rapidly
Positive cultures within 48-72 hr.
Generally not positive >48-72 hr. after lesion appears
Generally not positive if on acyclovir therapy

- Direct detection of virus
  - Less sensitive
  - Smears of lesions (detect 60-90%) (Pap smears)
    - Sensitivity 60%
    - Specificity 95%
    - Look for intranuclear inclusions.
  - Specific fluorescent, peroxidase in situ hybridization and ELISA (Herpchek) tests (70-98% sensitive)
  - Monoclonal antibody tests – 75% concordance with cultures
  - Tzanck prep for herpetic morphologic changes
    - Sensitivity 85%
    - Specificity 95%

- Serology
  - Limited to retrospective diagnosis of primary infection
  - ELISA, neutralization, fluorescent and indirect hemagglutination (IHA) tests have some cross reactions between HSV-1 and HSV-2
  - Most people have HSV-1 antibody and many have HSV-2 antibody
  - These tests cannot reliably distinguish between serotypes

H. Treatment
- Acyclovir interferes selectively with viral thymidine kinase
- Concentrated in HSV infected cells
- Active metabolite is acyclovir triphosphate
- Topical acyclovir
  - Topical 5% ointment effective only in primary HSV
  - Decreased duration of pain (6 vs 9 days)
  - Decreased viral shedding (4 vs 7 days)
  - Decreased mean time to healing (11 vs 12 days)
- Current CDC recommendations for acyclovir
  - Pregnancy – category B
ACYCLOVIR AS follows

<table>
<thead>
<tr>
<th>Clinical Episode</th>
<th>Treatment Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>First clinical episode</td>
<td>200 mg po 5 times/day x 7-10 days</td>
</tr>
<tr>
<td>Recurrent episodes</td>
<td>200 mg po 5 times/day x 5 days, or 400 mg po 3 times/day x 5 days, or 800 mg po 2 times/day x 5 days</td>
</tr>
<tr>
<td>Suppression</td>
<td>200 mg orally 2 to 5 times/day, or 400 mg orally 2 times/day</td>
</tr>
<tr>
<td>Severe disease</td>
<td>400 mg orally 2 times/day</td>
</tr>
</tbody>
</table>

- Other therapies
  - Vaccines – under investigation
  - Supportive care
    - Sitz baths
    - Topical anesthetics
    - Blow dryers on cool
  - Famciclovir
  - Valacyclovir
    - Improved bioavailability
    - Less expensive for a course of therapy
    - So far approved for recurrent episodes only
    - Pregnancy category B drug

I. HSV infection in HIV-infected patients
- Increased severity
- Frequency of reactivation increased
- Most common presentation
  - Chronic mucocutaneous ulceration
  - Pain and lesions persist for months
- HSV may be a risk factor for acquisition of HIV
- Treatment
  - Acyclovir – 400 mg 3-5 times/day x 14 days or until clinical resolution
  - Valacyclovir – may reduce duration of pain

J. Complications of HSV infection
- Meningitis
- Hepatitis
- Disseminated disease
- Neonatal HSV

K. Neonatal HSV
- Vesicular rash
- Nervous-system disease
  - Lethargy
Anorexia
Vomiting
Fever
Irritability

• Visceral organ dissemination without CNS involvement
  • Liver
  • Adrenals
• Asymptomatic infection
• Frequently fatal if untreated (the more disseminated, the higher the mortality)

L. Clinical take home
• HSV is a common STD
• Acyclovir can decrease viral shedding and symptomatology.
• During pregnancy, cesarean delivery for active lesions or prodrome only. No weekly cultures
• Consider prophylaxis daily beginning at 36 weeks gestation when patient has history of HSV

V. Rubella
A. History
• First described 1941
  • Gregg, Australian ophthalmologist
B. Frequency (vaccination programs began 1969)
• Before 1969
  • Major epidemic every 6-9 yr.
  • Last major epidemic 1964
• After 1969
  • Decreased major epidemics
  • Only 9 cases of congenital rubella syndrome in 1982
C. Incidence – rare
D. Clinical findings (evident in 2/3 of women)
• Within 2-3 wk. of exposure
• Three-day rash
  • Pink-red maculopapules
  • Face, trunk and extremities
• Lymphadenopathy
  • Suboccipital
  • Postauricular
  • Cervical
• Headache, fever, malaise, anorexia
• Conjunctivitis, cough
E. Laboratory findings
• Antibody seroconversion (ELISA)
• Rubella IgM antibody
• Isolate virus from throat

F. Congenital rubella syndrome (*most frequent finding)
• Cataracts
• *Congenital heart disease
  • Pulmonic stenosis
  • Patent ductus arteriosus
  • Ventricular septal defect
  • Myocarditis
• Congenital glaucoma
• Radiolucent bone lesions
• Hepatosplenomegaly
• Petechiae
• Thrombocytopenia
• *Hearing loss

G. Late-appearing defects in children
• Diabetes – 20% (age of onset 10-20 yr.)
• Thyroid disease – 5%
• Additional ocular damage – 3%

H. Laboratory diagnosis of congenital rubella
• IgM antibody during first 6-12 mo. of life
• Elevated IgG after 6 mo. persistent
• Viral isolation from nasopharynx

I. Antenatal diagnosis – cordocentesis
• Wks 20-26
• Rubella specific IgM

J. Prognosis
• Depends on extent of organ damage – time of exposure
  • First month – 50% have significant damage
  • Second month – 22% have significant damage
  • Third month – 10% have significant damage
  • Fourth or fifth month – 5-6% have significant damage
• United Kingdom study (after 1964 epidemic)
  • 1-12 wk. – 80%
  • 13-14 wk. – 54%
  • 15-16 wk. – 25%
  • 4% spontaneous abortion

K. Management
• Maternal – no specific treatment
  • Rest
  • Analgesics
• Child
  • Isolate virus
Clinical studies to determine damage
• Close follow-up

L. Prevention
• Vaccination
  • RA 27/3
  • Contraindicated in pregnancy (although no reports of fetal anomalies when given within 3 months of conception or during pregnancy)
• Immunize postpartum

VI. Group B streptococci (GBS)
A. Classification
• S. agalactiae

B. History
• First isolated 1887 Nocard
• Lancefield and Hare 1935
• Previously called S. mastititis

C. Microbiology
• Gram-positive cocci
• Grows in chains
• Colonies are smooth, shiny white mounds
• Antigen-specific groups = serologic types – Ia, Ib, Ic, II, and III

D. Laboratory
• β-hemolysis
• Bacitracin resistance
• Hippurate hydrolysis
• Enhancement of staphylococcal β-hemolysis

E. Epidemiology
• GI tract principal reservoir
• Normal vaginal flora
  • Colonization rates fecal > vaginal > cervical
  • Rates vary from 5-30%
  • Colonization rates increase if
    - Age < 20 yr.
    - Lower income
    - African American
    - Asymptomatic bacteriuria
    - Sexually active
  • Colonization rates decreased if:
    - Multiparity > 4
    - Hispanic
    - Caucasian
    - Private obstetric care
• Fetal colonization rates 50-75%
  • Generally ascending
  • Contamination via passage through birth canal
  • Factors
    - Heavy maternal colonization
    - ROM > 18°
    - Maternal fever or endometritis
    - Prolonged labor
    - Preterm delivery
• Neonatal attack rates
  • Early onset GBS Sepsis – 2-3/1000
  • Late onset GBS Sepsis – 0.5-1/1000

F. Spectrum of Disease
• UTI
  • Asymptomatic bacteriuria
  • Cystitis
  • Pyelonephritis
• Genital tract infection
  • Chorioamnionitis
  • Maternal septicemia
  • Postpartum endometritis
    - Abrupt onset
    - < 24 hr. postpartum
    - Temp > 102°F
    - Maternal tachycardia
    - Bacteremia common
• Neonatal disease (generally type III)
  • Early onset (during wk 1 of life)
    - Septicemia
    - Pneumonia
    - Meningitis
    - Respiratory distress
      - Apnea
      - Grunting
      - Tachypnea
      - Cyanosis
    - Other signs
      - Decreased BP
      - Lethargy
      - Poor feeding
      - Temperature instability
      - Abdominal distention
      - Pallor
      - Tachycardia
Jaundice

- Late onset (beyond 7 days of life and < 12 wk. of age)
  - Generally term infant
  - Fever
  - Irritability
  - Lethargy
  - Meningitis

### APPEARANCE OF NEONATAL GBS

<table>
<thead>
<tr>
<th>Feature</th>
<th>Early</th>
<th>Late</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>20 hr.</td>
<td>24 days</td>
</tr>
<tr>
<td>Preterm birth</td>
<td>Increased</td>
<td>No change</td>
</tr>
<tr>
<td>Obstetric complications</td>
<td>Frequent (60%)</td>
<td>Uncommon</td>
</tr>
<tr>
<td>Septicemia (40%)</td>
<td>Meningitis</td>
<td></td>
</tr>
<tr>
<td>Meningitis (30%)</td>
<td>Bacteremia</td>
<td></td>
</tr>
<tr>
<td>Pneumonia (40%)</td>
<td>Bone/joint infection</td>
<td></td>
</tr>
<tr>
<td>Manifestations</td>
<td>Ia, Ib/c, Ia/c (30%)</td>
<td>III (93%)</td>
</tr>
<tr>
<td>Serotypes</td>
<td>II (30%)</td>
<td></td>
</tr>
<tr>
<td>III (40%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Morbidity</td>
<td>10-20%</td>
<td>1%</td>
</tr>
</tbody>
</table>

- Risks for neonatal GBS sepsis
  - Prenatal GBS heavy colonization
  - Age < 20 yr.
  - Black
  - Lack of anti-GBS capsular antibody
  - GBS bacteriuria
  - Prior infant affected
- Factors associated with neonatal mortality
  - Low 5-minute Apgar
  - Shock or leukopenia
  - Prolonged ROM
  - Delay in treatment

G. Diagnosis
- Culture is gold standard
H. Treatment
  • Some regimens

<table>
<thead>
<tr>
<th>Site of Infection</th>
<th>Drug</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacteremia w/o meningitis</td>
<td>Ampicillin</td>
<td>150-200 mg/kg/d</td>
</tr>
<tr>
<td></td>
<td>Gentamicin</td>
<td>7.5 mg/kg/d</td>
</tr>
<tr>
<td>Meningitis</td>
<td>Ampicillin</td>
<td>300-400 mg/kg/d</td>
</tr>
<tr>
<td></td>
<td>Gentamicin</td>
<td>7.5 mg/kg/d</td>
</tr>
<tr>
<td>Septic arthritis</td>
<td>Penicillin G</td>
<td>200,000 U/kg/d</td>
</tr>
<tr>
<td>Osteomyelitis</td>
<td>Penicillin G</td>
<td>200,000 U/kg/d</td>
</tr>
<tr>
<td>Endocarditis</td>
<td>Penicillin G</td>
<td>400,000 U/kg/d</td>
</tr>
</tbody>
</table>

• Antibiotic resistance of GBS in pregnant women rare, but increasing

I. Strategies for preventing early-onset Group B Streptococcal neonatal sepsis
  • All gravidas – vaginal and rectal culture at 34-36 wk.
    If culture positive, treat in labor, or
    Gravidas with risk factors of:
  • Preterm labor, treat until culture status is known. If no culture available, treat for:
    • Prolonged rupture of membranes >18 hours
    • Intrapartum fever >100.4 degrees
    • Prior maternal UTI with GBS
    • Prior infant infected with GBS
  • Treat with intrapartum penicillin, other antibiotic if PCN allergic

VII. Hepatitis B Virus (HBV)
A. Epidemiology
  • 1/1000 adults in USA are infected
  • 4-13% of Southeast Asians are infected – 40-50% of chronic carriers may have been infected congenitally
  • Perinatal transmission can occur during chronic and acute infections
  • Transmission and chronic carrier risk vary
    • If HBsAg and HBeAg are both positive
      - 80-90% perinatal transmission
      - 90% infected infants will become chronic carriers
    • If HBsAg is positive, but HBeAg is negative
      - 10-25% perinatal transmission
      - Lower chronic carrier rate
  • 50% of chronic carriers will die from cirrhosis or liver cancer
B. Transmission
  • Can occur via
    • Blood
• Body fluids, including saliva
• Oral contact
• Sexual contact
• Fomites on shared items (towels, razors, washcloths, etc.)

• Risk factors
  • IV drug use
  • Multiple sexual partners
  • Sexual partner with multiple sexual partners
  • Homosexual partners or activity
  • Transfusions
  • Immigration from Southeast Asia
  • Health care worker

• About 1/2 of gravidas who are infected do not have a history of traditional risk factors

C. Clinical course
• Incubation 50-180 days
• Symptoms
  • Fever
  • Headache
  • Abdominal pain
  • Nausea and vomiting
  • Jaundice with dark urine
  • Hepatomegaly
  • Clinical improvement begins as jaundice resolves

• 10% will develop chronic disease
  • 7% chronic persistent (normal LFTs)
  • 3% chronic active (abnormal LFTs)

• Horizontal transmission can occur until antibody is present

D. Laboratory diagnosis
• Abnormal liver functions
  • ALT rises 50 days after exposure and stays elevated 30-60 days
  • AST rises

• Serology
  • HBsAg appears 30-50 days after exposure, about 7-21 days before onset of jaundice
  • HBeAg appears early and may persist indefinitely – increases likelihood of transmission
  • Presence of HBeAb decreases likelihood of transmission

E. Perinatal infection
• Risk of fetal/neonatal infection is greatest when mother was infected during third trimester or first 2 months postpartum
• Exposure most often occurs at delivery
  • Exposure through breast milk is also common
  • Transplacental infection – unusual, but possible (5%)
F. Management

- Screen all pregnant women (per CDC)
  - Vaccinate if patient is in a high-risk group and is not immune
    - Vaccination is NOT contraindicated during pregnancy
    - 3 doses – initial, 25-30 days later, 6 months later
- HBIG within 24 HR. if susceptible patient is exposed
  - Start vaccine series
  - HBIG + vaccine will prevent 75% of infections
- Treat acute infections with supportive care
- Blood and body fluid precautions during acute and chronic disease
- HBIG and vaccine to newborn
  - Within 48 HR. after birth (sooner for HBIG if possible)
  - Decreases chronic carrier risk by 90%
- HBIG and vaccine to newborn
  - Breast feeding is ok if infant received HBIG vaccine

G. Hepatitis A not a problem for infant – treat mother with supportive care.

H. Hepatitis C

- Similar in transmission, behavior and sequelae to Hepatitis B
- Often asymptomatic
- Most appropriate method of preventing and treating Hepatitis C not well delineated
  - Give HBIG and vaccine if exposed
    - Vaccine primarily because risk factors for B and C are same
    - Not clear whether HBIG is very helpful
  - Same for exposed neonate
- Routine screening not recommended unless patient has risk factors or history (past or current) or Hepatitis B

VIII. Human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome (HIV/AIDS)

A. Virology

- Nomenclature – human immunodeficiency virus (HIV)
- RNA virus
- Retrovirus – utilizes reverse transcriptase to transcribe DNA from RNA
- Tropic for CD4+ lymphocytes – weakens and ultimately destroys these cells, resulting in severe deficiency in cell-mediated immunity

B. Principal risk factors for homosexual or heterosexual transmission

- Multiple partners
  - Male-to-female transmission is ~ twice as efficient as female-to-male transmission
  - Risk of transmission varies with illness severity in index case
- Receptive anal intercourse
  - Concurrent I.V. drug use
• Crack cocaine use
• Ulcerated genital lesion infection
  · Herpes
  · Syphilis
  · Chancroid
• Uncircumcised male is more at risk of transmitting infection to partner

C. Classification of infection

<table>
<thead>
<tr>
<th>CDC CLASS</th>
<th>DESCRIPTION</th>
<th>SIZE OF VIRAL INOCULUM</th>
<th>REMARKS</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Acute HIV infection</td>
<td>Moderate</td>
<td>Occurs 3-6 wk. after exposure</td>
</tr>
<tr>
<td>II</td>
<td>Asymptomatic</td>
<td>Low</td>
<td>Median duration may be as high as 10 yr.</td>
</tr>
<tr>
<td>III</td>
<td>Generalized Lymphadenopathy</td>
<td>Moderate</td>
<td>Once this stage of illness is reached, life expectancy is ≤ 5 yr.</td>
</tr>
<tr>
<td>IV</td>
<td>AIDS</td>
<td>High</td>
<td></td>
</tr>
</tbody>
</table>

D. Laboratory diagnosis
• Viral culture
• Detection of viral antigen – of particular value in screening blood supply and in detecting neonatal infection
  · Antigen capture assay
  · Polymerase chain reaction
• Decreased number of CD4 cells and inverted CD4:CD8 ratio
• Elevated immunoglobulin levels (especially IgG)
• Detection of antibody to HIV-1
  · ELISA or HIV-1 EIA
  · HIV-1 Western Blot – test is considered positive when any 2 bands {p 24 (viral core), gp 41 (envelope), and gp 120/160 (envelope)} are present
• Detection of antibody to HIV-2
  · HIV-2 EIA
  · HIV-1/HIV-2 EIA
  · HIV-2 Western Blot
• Indications for HIV-2 testing
  · Sex partner or needle-sharing partner of persons from a country where HIV-2 infection is endemic
  · Person who received a transfusion or nonsterile injection in a country where HIV-2 infection is endemic
  · Children of high-risk women
Clinical evidence of HIV infection but serologic tests for HIV-1 are not confirmatory.

E. Perinatal considerations

- ~ 90% of all cases of HIV infection in children result from perinatal transmission.
  - ~ 15,000 infected infants were born in USA 1978 through 1993
  - ~ 1,600 new cases of perinatal transmission occur annually
  - 18% of infected children have now died

- Mechanisms of transmission
  - Transplacental
  - Intrapartum exposure to maternal blood and genital tract secretions
  - Breast milk
    - Previously, risk associated with breastfeeding was regarded as very low
    - Recent investigations suggest that risk of infection may be surprisingly high
      - In breastfeeding mothers infected postnatal, risk of transmission to infant is 29% (95% C.I. 16-42%)
      - In mothers infected prenatal, additional risk of transmission is 14% (beyond that occurring prenatal or intrapartum) (95% C.I. 7-22%)
  - Close personal contact after delivery – uncommon

- Frequency of transmission to neonate is 20-30%
  - Transmission decreases to 63% with zidovudine treatment of mother and neonate
Factors influencing vertical transmission

<table>
<thead>
<tr>
<th>RISK FACTOR</th>
<th>MECHANISM</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV&lt;sub&gt;1&lt;/sub&gt; &gt; HIV&lt;sub&gt;2&lt;/sub&gt;</td>
<td>HIV&lt;sub&gt;1&lt;/sub&gt; is more virulent than HIV&lt;sub&gt;2&lt;/sub&gt;</td>
</tr>
<tr>
<td>Previous child with AIDS</td>
<td>Higher viral inoculum in mother</td>
</tr>
<tr>
<td>Overt AIDS in mother</td>
<td>Higher viral inoculum in mother</td>
</tr>
<tr>
<td>Prematurity</td>
<td>Decreased immune defenses in neonate</td>
</tr>
<tr>
<td>Decreased CD4 count</td>
<td>Impaired maternal defenses</td>
</tr>
<tr>
<td>p24 antigenemia</td>
<td>Higher viral inoculum in mother</td>
</tr>
<tr>
<td>First twin</td>
<td>Greater exposure to infected maternal blood and genital tract secretions</td>
</tr>
<tr>
<td>Chorioamnionitis</td>
<td>Vascular injury within placenta increases probability of viral transmission</td>
</tr>
<tr>
<td>Increased intrapartum blood exposure</td>
<td>Higher viral inoculum</td>
</tr>
<tr>
<td>Ruptured membranes &gt; 4 hr.</td>
<td>Prolonged exposure to virus and higher viral inoculum</td>
</tr>
</tbody>
</table>

- Obstetric complications in AIDS patients
  - Increased frequency of preterm delivery
  - Increased frequency of IUGR
  - Increased frequency of stillbirth
  - Increased neonatal mortality
  - Increased frequency of puerperal endometritis
- Pregnancy does not seem to accelerate course of HIV infection. Overall, natural history of HIV infection worse in women. When maternal mortalities occur, usually due to *P. carinii* infection.

F. Obstetric management
- Prenatal care
  - **Universal screening** of pregnant women is justified.
  - Counseling for seropositive women
    - Advise that frequency of perinatal transmission is ~ 20-30%. Revised estimate upward if risk factor present.
    - Advise that risk of transmission decreases markedly with zidovudine protocol
    - Indicate that pregnancy termination is an option patient may wish to consider
    - Screen for other sexually-transmitted diseases
  - Screen for CMV
  - Screen for toxoplasmosis
  - Screen for tuberculosis. Must do companion testing for allergy
with 2 skin tests (candida, mumps, tetanus toxoid).

- Vaccination against infection by HBV, pneumococcus, influenza and *Hemophilus influenza*

<table>
<thead>
<tr>
<th>VACCINE</th>
<th>RESPONSE (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pneumococcal</td>
<td>88</td>
</tr>
<tr>
<td><em>H. influenza</em> B</td>
<td>97</td>
</tr>
<tr>
<td>Influenza</td>
<td>50-90</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>25-60</td>
</tr>
</tbody>
</table>

- Assess cervical cytology
- Encourage patient to discontinue smoking, which appears to accelerate decline in CD$_4$ count.
- Treating asymptomatic women
  - Benefits
    - Reduce risk of vertical transmission
    - Viral load reduction
    - Delay AIDS
    - Preserve immune function
  - Risks (potential)
    - Poor quality of life
    - Earlier drug resistance
    - Limits future therapy
    - Spread resistant HIV
    - Long-term toxicity unknown
  - Indications for treatment
    - Symptomatic
    - CO4 < 500; RNA > 10,000
    - CD4 > 500; RNA < 10,000 – may observe
- Pregnant women: Zidovudine protocol
  - For asymptomatic women
  - Start Zidovudine at 12-13 wk.
  - Continue through pregnancy
  - IV therapy during labor
  - Treat newborn for 6 wk.
  - Consider adding another drug to decrease resistance
  - For women with low CD4 or symptoms, treat as indicated by disease status
- Prophylaxis for selected opportunistic infections
<table>
<thead>
<tr>
<th>CONDITION</th>
<th>INDICATION FOR PROPHYLAXIS</th>
<th>ANTIBIOTIC REGIMEN</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Pneumocystis carinii</em> pneumonia</td>
<td>Prior infection or CD&lt;sub&gt;4&lt;/sub&gt;&lt;200/mm&lt;sup&gt;3&lt;/sup&gt;</td>
<td>TMP-SMX-1 DS tablet Q.D. indefinitely</td>
</tr>
<tr>
<td>Toxoplasmonic encephalitis</td>
<td>CD&lt;sub&gt;4&lt;/sub&gt;&lt;100/mm&lt;sup&gt;3&lt;/sup&gt; + serology</td>
<td>TMP-SMX-1 DS tablet Q.D. indefinitely</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>+PPD &gt;5mm</td>
<td>INH, 300 mg Q.D., plus pyridoxine, 50 mg Q.D., x 12 mo.</td>
</tr>
<tr>
<td>Disseminated infection with <em>Mycobacterium avium</em> complex</td>
<td>CD&lt;sub&gt;4&lt;/sub&gt;&lt;75/mm&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Rifabutin-300 mg Q.D. indefinitely</td>
</tr>
<tr>
<td>Cryptococcosis</td>
<td>CD&lt;sub&gt;4&lt;/sub&gt;&lt;50/mm&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Fluconazole-100 to 200 mg Q.D. indefinitely</td>
</tr>
</tbody>
</table>

Ref: MMWR 1995;44:1-34.

- Intrapartum care
  - Avoid scalp electrode
  - Use mechanical suction to clear neonate’s airway
  - Cesarean delivery to prevent neonatal transmission, if high maternal viral load
  - Double glove
  - Avoid rupture of membranes
  - ZDV – protease inhibitors under investigation

- Postpartum care
  - Avoid breastfeeding
  - Prevent contact between maternal body fluids and neonate
  - Utilize effective contraception
  - Adopt responsible sexual practices

G. Summary
- Virology – RNA retrovirus
- Mechanisms of transmission
  - Sexual contact
  - Parenteral
  - Perinatal
- Diagnosis
  - Detection of antibody
  - Detection of antigen
  - Culture of virus
- Frequency of perinatal transmission – 20-30%
- Prevention of vertical transmission – Prophylactic ZDV for mother and neonate
- Prevention of horizontal transmission
  - “Safe sex”
Avoidance of IVDU
Universal precautions for health care workers

IX. Human papillomavirus (HPV) infection
A. Organism – human papillomavirus
   • At least 70 serotypes
   • 6, 11 associated with genital warts
   • 16, 18, 31, 33, 35, 45, 51, 52, and 56 associated with high-grade
dysplasia and cancer
   • More than 30% of sexually active females have been exposed to virus
B. Clinical findings
   • Flat condyloma, condyloma acuminata – tend to enlarge/spread in
pregnancy
   • Cervical, vaginal and vulvar intraepithelial neoplasia
   • Asymptomatic
C. Diagnosis
   • Clinical exam
   • Biopsy
   • DNA hybridization (? PCR)
D. Treatment
   • Patient-applied
     • Imiquimod 5% cream qHS x 3 days/wk (not approved for use in
pregnancy)
   • Provider-administered
     • Cryotherapy
     • TCA 85%
     • Surgical removal
       - Local excision
       - Curettage
       - Electrosurgery
       - Laser
     • Interferon
E. Perinatal issues – no need to perform cesarean for prevention of laryngeal
papillomatosis

X. Other STDs
A. Syphilis
   • Organism – Treponema pallidum
   • Clinical findings
     • Primary
       - Painless ulcer
       - Site of inoculation
       - 10-90 days after exposure
       - Macule → ulcer – sharp, erythematous, demarcated base
Secondary – rash
  - Mucocutaneous lesions
  - Adenopathy
  - Rash may involve soles/palms

Latent – asymptomatic
  - Early – < 1 yr. duration
  - Late – > 1 yr. duration

Tertiary – untreated syphilis – 1 of 3 will develop
  - CNS
  - Cardiovascular
  - Musculo-skeletal

• Diagnosis
  • Primary – positive darkfield examination
  • Secondary
    - Positive darkfield examination
    - Serology positive
  • Latent – serologic testing
    - Screen
      - RPR (Rapid Plasma Reagin)
      - VDRL (Venereal Disease Reference Laboratory)
    - Specific test
      - FTA-ABS (Fluorescent Treponemal Antibody – absorbed)
      - MHA-TP (Microhemagglutination Assay)

• Treatment
  • Primary, secondary, early latent – Benzathine penicillin 2.4 mU IM
  • Late latent, unknown duration – Benzathine penicillin 2.4 mU IM x 3 doses
  • Penicillin desensitization in pregnancy

• Perinatal issues
  • Congenital syphilis
    - Asymptomatic
    - Symptomatic
      - Macular papular rash
      - Bullae
      - Mucous patches
      - Rhinitis
      - Hepatosplenomegaly
      - Jaundice
      - Edema
      - Deformed nails
      - Alopecia
      - Fever
- Chorioretinitis
- Iritis
- Treatment – CSF evaluation
  - If normal – Benzathine penicillin G – 50,000 IM
  - If abnormal – Penicillin 50,000 u/kg daily divided into two doses x 10 days
  - Jarisch-Herxheimer reaction
    - Fever
    - Headache
    - Malaise
    - Contractions
    - Late decelerations

B. Chancroid
- Etiology – *H. ducreyi*
- Clinical findings
  - Painful genital ulcers
  - Regional lymphadenopathy
  - Dysuria
  - Dyspareunia
  - Rectal bleeding
  - Vaginal discharge
- Diagnosis
  - Clinically
    - Ulcer with ragged, undermined edges
    - Sharply demarcated
    - No induration
  - Laboratory
    - Isolate *H. ducreyi*
    - Needs special media
- Treatment
  - Azithromycin 1 gm
  - Ceftriaxone 250 mg IM
  - Ciprofloxacin 500 mg BID x 3 days
  - Erythromycin 500 mg QID x 7 days

C. Granuloma inguinale
- Etiology – *Calymmatobacterium granulomatis*
- Clinical findings
  - Painless progressive ulcers
  - No regional lymphadenopathy
  - Very vascular
- Diagnosis – Donovan bodies on staining
- Treatment
  - Trimethoprim-sulfamethoxazole BID x 3 wk.
  - Doxycycline 100 mg BID x 3 wk.
Ciprofloxacin 750 mg BID x 3 wk.
Erythromycin 500 mg po QID x 3 wk.

XI. Cytomegalovirus (CMV)
A. Incidence
- 1-2% of all live births (most common congenital viral infection in USA)
- 30,000-40,000 infants/yr. born with congenital viral infection in USA

B. Maternal symptoms
- Asymptomatic
- Mononucleosis-like illness (heterophile-negative)
  - Pharyngitis
  - Fatigue
  - Malaise
  - Fever
  - Lymphadenopathy (may be positive up to 60 days)
- Hepatitis

C. Diagnosis and management
- Mother
  - ELISA or fluorescent antibody (FA) – IgM specific
  - Viral cultures – maternal urine and cervix “gold standard” and most specific
  - In situ hybridization and polymerase chain reaction – experimental
- Infant
  - Serology – CMV-IgM antibody
  - Viral cultures of urine, nasopharynx, conjunctiva, CSF

D. Frequency
- CMV antibodies – present in 40-100% adults
  - Lower socioeconomic classes more likely to have previous CMV (85%).
  - Lower class more likely to have recurrent infection during pregnancy.
  - Middle/upper class more likely to have primary disease (only about 50% immune).
- Primary infection occurs in 1-2% of pregnant women.
- CMV can be isolated from 3% of women at term.

E. Transmission
- Direct contact
- Blood transfusion
- Perinatal

F. Congenital CMV
- Most infants are asymptomatic
- If symptomatic,
  - Hepatosplenomegaly
- Thrombocytopenia
- Petechiae
- Jaundice
- Mental retardation
- Sensorineural hearing loss
- Microcephaly
- Other sequelae

### SEQUELAE* OF CONGENITAL CMV INFECTION

**BY TYPE OF MATERNAL INFECTION**

<table>
<thead>
<tr>
<th>SEQUELA</th>
<th>PRIMARY (N=125)</th>
<th>RECURRENT** (N=64)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hearing loss</td>
<td>15%</td>
<td>5%</td>
<td>0.05</td>
</tr>
<tr>
<td>Bilateral hearing loss</td>
<td>8%</td>
<td>0%</td>
<td></td>
</tr>
<tr>
<td>IQ ≤ 70</td>
<td>13%</td>
<td>0%</td>
<td>0.03</td>
</tr>
<tr>
<td>Chorioretinitis</td>
<td>6%</td>
<td>2%</td>
<td>NS</td>
</tr>
<tr>
<td>Microcephaly</td>
<td>5%</td>
<td>2%</td>
<td>0.25</td>
</tr>
<tr>
<td>Seizures</td>
<td>5</td>
<td>0</td>
<td>0.08</td>
</tr>
<tr>
<td>Death (after NB)</td>
<td>2</td>
<td>0</td>
<td>NS</td>
</tr>
<tr>
<td>Any</td>
<td>25</td>
<td>8</td>
<td>0.003</td>
</tr>
</tbody>
</table>

G. Perinatal transmission
- Primary infections – 50%
- Secondary infection – 0.5-2.0%

H. Prenatal diagnosis
- Amniocentesis
- Amniocentesis plus fetal blood sampling
- Amniotic fluid culture and PCR

I. Treatment
- Mother – treat symptoms only
- Infant – no specific treatment, Acyclovir and Vidarabine are experimental; ganciclovir may be used

J. Prevention
- Live attenuated CMV vaccine (Towne strain) – used only in renal transplant patients
- Minimize risk of exposure in susceptible women

XII. Toxoplasmosis
A. Etiology – *Toxoplasma gondii*
B. Seroprevalence – 3-30%
C. Acute maternal infection – 0.2-1%
D. Acute congenital infection – 0.01-0.1%
E. Life cycle
• Host – cats
• Intermediate hosts – man, rodents, sheep
• Human infestation
  • Contacting infected cat feces
  • Eating poorly cooked meats

F. Clinical findings – maternal
• Generally asymptomatic
• Mononucleosis-like illness
  • Lymphadenopathy (10-20%)
  • More likely with acute disease
• Ocular manifestations
• ± virulent course in HIV-positive patients

G. Diagnosis
• Bioassays
  • Take 6 wk.
  • Infected blood injected into mice
• Serology
  • IgM ± for 6 mo.
  • Rising IgG titers can confirm recent infection.

H. Prenatal diagnosis
• Amniocentesis (at least 4 wk. after mother's infection)
  • Isolate organism
  • DNA-PCR – sensitivity about 100%
• Cordocentesis
  a. Isolate organism
  b. Toxo IgM
    no longer recommended
• Sonography

I. Neonatal toxoplasmosis
• Incidence – 10/20,000 pregnancies
• Etiology – perinatal transmission
  • First trimester – 15% (75% severe or stillborn)
  • Second trimester – 30% (20% severe or stillborn)
  • Third trimester – 60% (0% severe or stillborn)
• Clinical findings
  • Chorioretinitis
  • Convulsions
  • Hydrocephaly
  • Microcephaly
  • Jaundice
  • Fever
  • Hepatosplenomegaly
  • Lymphadenopathy
• Pathogenesis of congenital infection

• Diagnosis
  • Serology IgM; Sabin-Feldman dye test (reference test) primarily measures IgG
  • Non-specific findings
    - Abnormal CSF
    - Anemia
    - Intracranial calcifications
    - Thrombocytopenia

J. Management

• Mother – specific treatment generally unnecessary. If needed:
  • Pyrimethamine 25 mg po qd plus sulfadiazine (1 gm po QID) or triple sulfa
  • Concurrently give folinic acid 6 mg IM or orally x 3/wk.
  • Spiramycin may be obtained from FDA in select cases

• Prevention
  • Cook meat to well done, smoke it or cure it in brine
  • Avoid touching mucous membranes of mouth and eyes while handling raw meat
  • Wash hands thoroughly after handling raw meat
  • Wash kitchen surfaces that have contact with raw meat
  • Wash fruits and vegetables before consumption
  • Prevent access of flies, cockroaches, etc. to fruits and vegetables.
  • Avoid contact with materials potentially contaminated with cat feces, such as litter boxes, or wear gloves when handling such materials or when gardening
  • Disinfect cat litter box for 5 min. with boiling water, or line litter box with the bag litter comes in; then the box does not come in contact with used litter, and mess is prevented, not boiled away

XIII. Varicella

A. Epidemiology

• Congenital varicella is unusual – 13/100,000 live births
• Risk of teratogenic effects is <1% – almost all cases occur when gestation is < 20 wk.
• Congenital varicella may rarely be caused by herpes zoster

B. Diagnosis/clinical course

• Incubation 10-20 days – transmission by direct/indirect contact, as well as through respiratory droplets
• Presenting symptoms – fever, malaise and rash
  • Rash starts on trunk and moves to extremities and face
  • Papules become vesicles, eventually crust over
  • Intensely pruritic
• Diagnosis is confirmed with viral isolation or serology
• 75% of patients who cannot describe a history of varicella will be immune
• Immune status needs to be confirmed by checking varicella IgM and IgG
  • Negative for IgM and IgG – susceptible
  • Positive for IgM, negative for IgG – very recent infection (< few wk.)
  • Positive for IgM and IgG – recent infection (< few mo.)
  • Negative for IgM, positive for IgG – Immune
• 14% adults will get varicella pneumonia – may be higher in pregnancy
• 3% of those adults will die

C. Congenital varicella infection
• If maternal infection occurs at < 20 wk. gestation – < 1% chance of teratogenic effects
  • Skin scarring
  • Muscle atrophy
  • Hypoplastic extremities
  • Chorioretinitis
  • Encephalitis
  • Cortical atrophy
• Maternal infections occurring later in pregnancy may result in child having herpes zoster later in childhood
• If symptomatic maternal infection occurs between 5-21 days before delivery, infant may have mild chickenpox at birth
• If symptomatic maternal infection occurs between 5 days before delivery and 2 days after delivery, infant infection may be severe
  • Severe chickenpox
  • 30% neonatal demise

D. Management
• VZIG should be considered if mom confirmed to be susceptible and was exposed to varicella within last 96 hr.
  • Expensive
  • 5 vials generally necessary for adult
  • May decrease risk of infection or severity of disease
  • Unclear whether it decreases risk of fetal infection if mother is infected
• Contact and respiratory isolation from susceptible people
• Acyclovir for life-threatening infections – may see used more routinely in future
• VZIG to infant if mother has had clinical infection from 5 days before delivery to 2 days after delivery
  • Give within 72 hr. of birth
  • Not 100% protective
• No contact between mother and child until all of mother’s vesicles are dried

XIV. Parvovirus
A. Parvovirus infection – first discovered by Cosart and associates in 1975
B. Immunology

<table>
<thead>
<tr>
<th>AGE (YR.)</th>
<th>% IGG SEROPOSITIVE</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 5</td>
<td>2 - 9</td>
</tr>
<tr>
<td>5 - 18</td>
<td>15-35</td>
</tr>
<tr>
<td>&gt; 18</td>
<td>30-60</td>
</tr>
</tbody>
</table>

C. Clinical entities
• Dermatologic – erythema infectiosum (fifth disease)
  - Incubation – 4-20 days
  - Symptoms
    - Malaise
    - Sore throat
    - Coryza
    - Low-grade fever
    - Facial rash – bright erythematous, macular rash spreads to neck and trunk usually lasts less than 10 days.
    - Macular rash, arthralgias in adults
• Hematologic
  - Mild anemia
  - Transient aplastic crisis (TAC)
  - Chronic anemia
• Rheumatologic – arthralgia in adults common

D. Pregnancy associated parvovirus
• Non-immune hydrops fetalis
• Fetal death (stillbirth)
• Spontaneous abortion
• Myocarditis

E. Pathogenesis
• Rash – unknown
• Fetal death and hydrops – ? anemia

F. Epidemiology
• Occurs worldwide
• Incubation period 4-14 days
• Transmission
  - Respiratory secretion – direct contact
  - Parenterally
  - Vertical (mother to fetus)
G. Diagnosis

- B19 antibody assays
  - IgM most sensitive – indicates recent infection
  - IgG present by seventh day of illness
- Culture
  - Logistically not available.
  - Can grow in bone marrow explant cultures
- DNA analysis
  - Southern blot
  - In situ hybridization
  - Polymerase chain reaction

H. High Risk Groups

- Immunocompromised persons
- Persons with chronic hemolytic anemias
- Pregnant women

I. Prevention

- No active vaccine
- Routine prophylaxis with IgG not recommended
- Health care setting
  - No isolation for patients with erythema infectiosum
  - Isolate persons with TAC (Transient Aplastic Crisis)

J. Management in pregnancy

- Known infection – MSAFP, serial ultrasounds
- Fetus with anemia-intrauterine
- Pregnant women exposed to B19 parvovirus

Test for B19-specific IgG

[Diagram]

- Stop; patient immune
- Counsel risk relative to type of exposure (20-50%); if symptoms, test for B19-specific IgM

- Very likely not B19 infection
- Counsel risk for fetal infection/ disease (5%); do weekly U/S; if hydrops present, consider
XV. Cardiac disease
   A. Counseling
      • Successful pregnancy outcome depends upon
         • Functional capacity of the heart
         • Complications increasing cardiac load (hemorrhage, infection)
         • Quality of medical care
         • Social support
      • Counseling depends upon
         • Functional status
         • Specific lesion
         • Risk of congenital heart disease for fetus
      • Functional status
         • Functional classification not influenced by physical signs
         • New York Heart Association Classification (1979)
            – Class I – uncompromised, no limitation of physical activity, prognosis good
            – Class II – slightly compromised, comfortable at rest, discomfort with ordinary activity, prognosis good
            – Class III – markedly compromised, comfortable at rest, discomfort with less than ordinary activity, prognosis guarded
            – Class IV – severely compromised, cannot perform any physical activity without symptoms, may have symptoms at rest, prognosis poor
         • Generally, women in class I, and most class II, go through pregnancy without morbidity
         • However, up to 40% developing heart failure are Class I
- Mortality risk – ACOG Three-Tiered Classification (1992)

<table>
<thead>
<tr>
<th>GROUP</th>
<th>CARDIAC DISORDER</th>
<th>MORTALITY</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td>0-1%</td>
</tr>
<tr>
<td></td>
<td>Atrial-septal defect</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ventricular septal defect</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Patent ductus arteriosus</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pulmonic or tricuspid disease</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fallot tetralogy, corrected</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Bioprosthetic valve</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mitral stenosis, NYHA Class I and II</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td></td>
<td>5-15%</td>
</tr>
<tr>
<td></td>
<td>A Mitral stenosis, NYHA class III and IV</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Aortic stenosis</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Aortic coarctation without valve involvement</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fallot tetralogy, uncorrected</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Previous myocardial infarction</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Marfan syndrome, normal aorta</td>
<td></td>
</tr>
<tr>
<td></td>
<td>B Mitral stenosis with atrial fibrillation</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Artificial valve</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td></td>
<td>25-50%</td>
</tr>
<tr>
<td></td>
<td>Pulmonary hypertension</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Aortic coarctation with valve involvement</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Marfan syndrome with aortic involvement</td>
<td></td>
</tr>
</tbody>
</table>

- Fetal risks for CHD (congenital heart disease)
  - Overall incidence 0.5-1.0%
  - 40% have other associated anomalies
Most common congenital heart defects at birth

<table>
<thead>
<tr>
<th>HEART DEFECT</th>
<th>AVERAGE (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>VSD</td>
<td>28</td>
</tr>
<tr>
<td>PS</td>
<td>10</td>
</tr>
<tr>
<td>PDA</td>
<td>9</td>
</tr>
<tr>
<td>VSD with PS</td>
<td>7</td>
</tr>
<tr>
<td>ASD</td>
<td>7</td>
</tr>
<tr>
<td>AS</td>
<td>4</td>
</tr>
<tr>
<td>Coarctation</td>
<td>4</td>
</tr>
<tr>
<td>TGA</td>
<td>3</td>
</tr>
<tr>
<td>All others</td>
<td>11</td>
</tr>
</tbody>
</table>

Affected fetuses are only concordant for maternal lesion in up to 50% of cases

Multifactorial
- Atrial-septal or ventriculoseptal defect (ASD/VSD)
- Patent ductus arteriosus (PDA)
- Tetralogy of Fallot (TOF)
- Pulmonary or arterial stenosis (PS/AS)
- Coarctation of aorta
- Recurrence risk if parent or sibling affected (%)

<table>
<thead>
<tr>
<th>DEFECT</th>
<th>FATHER (%)</th>
<th>MOTHER (%)</th>
<th>1 SIBLING (%)</th>
<th>2 SIBLINGS (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>VSD</td>
<td>2</td>
<td>6-10</td>
<td>3</td>
<td>10</td>
</tr>
<tr>
<td>ASD</td>
<td>1.5</td>
<td>4-4.5</td>
<td>2.5</td>
<td>8</td>
</tr>
<tr>
<td>TOF</td>
<td>1.5</td>
<td>2.5</td>
<td>2.5</td>
<td>8</td>
</tr>
<tr>
<td>PS</td>
<td>2</td>
<td>4-6.5</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>AS</td>
<td>3</td>
<td>13-18</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>Coarctation</td>
<td>2</td>
<td>4</td>
<td>2</td>
<td>6</td>
</tr>
</tbody>
</table>

Autosomal recessive
- Ellis van Creveld (chondroectodermal dysplasia) – single atrium or ASD
- Meckel-Gruber
- Mucopolysaccharidosis (IV and VI)
- Refsum
- Cardioauditory syndrome

Autosomal dominant
- Ehlers-Danlos
- Marfan
- Neurofibromatosis
- Noonan
- Teacher-Collins
- Waardenburg
- IHSS
• X-linked
  - Duchenne muscular dystrophy
  - Ehlers-Danlos(V)
  - Hunter's
  - Focal dermal hypoplasia (Goltz)
• Chromosomal
  - Trisomy (13,18,21) – VSD, ASD, PDA
  - Triploidy – VSD, ASD
  - Deletions (5p) – Cri du chat, VSD
  - Monosomy X (45X) – coarctation, VSD, bicuspid aortic valve
• Maternal disease
  - Diabetes (3-5%) – VSD, coarctation, TGA
  - Lupus – complete heart block
  - PKU (25-50%) – VSD, ASD, tetralogy
  - Rubella (35%) – VSD, ASD, PDA
• Drug exposure
  - Lithium – probable increase in Ebstein anomaly (2.7%), tricuspid atresia
  - Alcohol (30%) – VSD, ASD, PDA
  - Dilantin – PS, AS, coarctation, PDA
  - Thalidomide – variable

B. Structural congenital lesions
• Endocarditis prophylaxis
  • Incidence of bacteremia 5-10%
  • Subacute bacterial endocarditis (SBE) usually due to low-virulence bacterial infection superimposed on an underlying lesion
    - Viridans streptococci
    - Group D streptococcus
    - Others including group B strep, group A β-hemolytic strep, pneumonia, Staphylococcus aureus, N. gonorrhoeae
  • AHA Guidelines for SBE prophylaxis based on low-, moderate-, or high-risk nature of procedure and type of heart lesion
  • New AHA Guidelines (1998)

http://216.185.112.5/presenter.jhtml?identifier=1729

<table>
<thead>
<tr>
<th>PROCEDURES FOR WHICH PROPHYLAXIS NOT RECOMMENDED</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaginal hysterectomy*</td>
</tr>
<tr>
<td>Vaginal delivery*</td>
</tr>
<tr>
<td>Cesarean delivery</td>
</tr>
<tr>
<td>In uninected tissue</td>
</tr>
</tbody>
</table>

46
Urethral catheterization
Uterine dilatation and curettage
Therapeutic abortion
Sterilization procedures
Insertion or removal of intrauterine devices

*prophylaxis optional for high-risk patients

- Congenital lesions
  - Atrial septal defect (ASD) – most common congenital heart lesion seen during pregnancy
    - Most are asymptomatic
    - Pregnancy, labor and delivery generally well tolerated
    - Murmur is inconspicuous, but second heart sound is split in expiration as well as inspiration
    - ECG – incomplete right bundle branch block
    - Echocardiography confirms diagnosis
    - Two rare, but potentially significant, complications
      - Arrhythmia’s (usual onset 4th decade; rare in pregnancy)
        - Atrial fibrillation most common, SVT, and atrial flutter
        - Treatment – initially digoxin, less often propranolol, quinidine, cardioversion may be necessary
        - Congestive heart failure (CHF) – hypervolemia of pregnancy may increase left-to-right shunt through ASD
          - CHF and death have been reported
    - Pulmonary pressures low, therefore, pulmonary HTN rare
    - Intrapartum fluid restriction
    - SBE prophylaxis (although at low risk)
    - Paradoxical embolus – originating in pelvic/leg veins to IVC across ASD to system circulation
    - Leg care and ambulation postpartum
  - Ventricle septal defect (VSD)
    - Isolated or in conjunction with other defects
    - Size is most important determinant or prognosis
    - Small defects tolerated well
    - On exam, loud pansystolic murmur along left sternal border with a course thrill
    - ECG may be normal
    - Echocardiography confirms diagnosis
- Large defects associated with aortic regurgitation, CHF, arrhythmia’s, pulmonary HTN
- Pregnancy, labor and delivery usually tolerated well
- Maternal deaths usually in setting of pulmonary HTN
- Intrapartum fluid restriction, SBE prophylaxis
  - Patent ductus arteriosus (PDA)
    - Uncommon during pregnancy due to detection and closure in neonatal period
    - Continuous “machinery” murmur
    - Like ASD and VSD, most women asymptomatic and tolerate pregnancy, labor and delivery well
    - Like VSD, large defects can lead to increased left-to-right shunt and pulmonary HTN
    - Maternal deaths usually in setting of pulmonary HTN; murmur may disappear
  - Eisenmenger syndrome
    - Presence of congenital left-to-right shunt (ASD, VSD, PDA) leads to progressive pulmonary HTN leading to shunt reversal (right-to-left) or bi-directional shunting
    - Pulmonary HTN carries grave prognosis – maternal mortality 30-50%
    - Medically indicated therapeutic termination may be offered.
- Coarctation of aorta
  - Most common site is at origin of left subclavian artery
  - Associated anomalies include VSD, PDA, aneurysms of circle of Willis, bicuspid aortic valve
  - Usually asymptomatic – HTN limited to upper extremities, is suggestive of diagnosis
  - Late systolic murmur over interscapular region
  - Chest x-ray reveals notching of inferior rib borders
  - ECG – left ventricular hypertrophy
  - Aneurysms may develop below coarctation or involve intercostal arteries
  - Death may be due to aortic dissection/rupture, CHF, CVA, endocarditis
  - Women with uncomplicated coarctation – NYHA Class I or II – good prognosis (3-4% mortality)
  - Aneurysms or associated cardiac lesions increase mortality risk up to 15%
  - Intrapartum management depends upon associated lesions
  - SBE prophylaxis
- Tetralogy of Fallot – most common form of cyanotic congenital heart disease encountered in pregnancy
Complex of
- VSD
- Overriding aorta
- RVH
- Pulmonary stenosis

Most corrected in childhood and, if corrected, have relatively good pregnancy outcome

15% mortality if uncorrected

Women may present with cyanosis and clubbing

On exam a loud, long systolic murmur is audible along left sternal border

ECG – right-ventricular hypertrophy

Pregnancy can worsen R → L shunt

Poor prognostic factors
- Hct > 65
- History of syncope or CHF
- EKG with evidence of RV strain
- Peripheral O₂ saturation < 80%
- Cardiomegaly
- RV pressure > 120 mmHg

Pulmonary stenosis
- May be valvular, supra- or subvalvular
- Degree of obstruction (not site) is principal determinant of maternal outcome
- Diagnosis suggested by long, harsh systolic murmur over pulmonary area
- Transvalvular pressure gradient > 80 mmHg requires surgical intervention
- Severe stenosis may lead to right heart failure

C. Acquired cardiac lesions

Overview
- Causes
  - Most are rheumatic in origin
  - Endocarditis secondary to IVDA (esp. right heart)
- Morbidity and mortality due to CHF or arrhythmia’s
- Pulmonary edema #1 cause of death

Pulmonic/Tricuspid
- Isolated right heart lesions rare with rheumatic disease – more likely due to IVDA and valvular endocarditis
- Usually well tolerated, PA catheter not needed
- Watch fluids, SBE prophylaxis

Mitral stenosis
- The most common rheumatic valvular lesion encountered during pregnancy
- Mitral valve area normal 4-6 cm²
- Symptoms occur at an area ~ 2 cm²
- Severe < 1 cm² requires surgery

• Symptoms
  - Left-sided heart failure
    - Dyspnea on exertion
    - Orthopnea
    - Paroxysmal nocturnal dyspnea
  - Less frequently, right-sided failure
    - Hemoptysis
    - Hoarseness

• Diagnosis
  - Physical exam
    - Classic diastolic rumble following opening snap
    - Loud S¹
  - Echocardiography confirms diagnosis

• Obstruction to left ventricular diastolic filling, i.e. fixed cardiac output
• CO increases of normal pregnancy may lead to pulmonary edema
• CO depends on
  - Adequate diastolic filling time
    - Avoid tachycardia (can cause fall in CO and BP)
    - Propranolol 20-40 mg q4-6h
    - Prevent/treat infection
    - Avoid acute blood loss
    - Pain control – epidural
  - Adequate left ventricular preload
    - Adequate fluids
    - Avoid diuretics
    - Avoid spinal anesthesia

• Most hazardous time is immediately postpartum
  - Highest CO
  - Postpartum rise in pulmonary wedge pressure up to 16 mmHg
  - Pulmonary edema occurs with wedge pressure 28-30 mmHg – optimal delivery wedge ~ 14 mmHg or lower
  - Anticipate “autotransfusion”

• Mitral valve prolapse/mitral insufficiency
  - Incidence ~ 5-10% of young women
  - Symptoms
    - Most asymptomatic
    - Arrhythmias
    - Syncope
Peripheral emboli
- Chest pain
- Palpitations
  
  Diagnosis
  - Late systolic murmur
  - Mid- or late-systolic “click”
  - Echocardiography
  
  Treatment
  - None, if asymptomatic
  - β-blockers if symptomatic
  - SBE prophylaxis

- **Aortic stenosis**
  - Usually idiopathic resulting from degeneration and calcification of aortic leaflets
  - During pregnancy, may be rheumatic and in conjunction with other lesions
  - ~ 5% of all congenital cardiac lesions
  - Normal valve area 2.6-3.5 cm²
  - Symptoms occur at 1/3 of normal area
  - Severe < 0.8 cm² or gradient > 100 mmHg
  - Classic symptoms are angina, syncope, symptoms of CHF
  - Signs – systolic ejection murmur radiation to neck
  - Diagnosis – echocardiography with Doppler
  - CO relatively fixed, i.e., preload critical
  - During exertion, CO may become inadequate to maintain coronary artery or cerebral perfusion leading to angina, MI syncope, sudden death
  - Marked limitation of physical activity is essential with severe disease
  - Termination of pregnancy and during delivery are times of greatest risk
  - Avoid hypotension from blood loss, ganglionic blockade (spinal/epidural), SVC occlusion by pregnant uterus in supine position
  - Consider pulmonary artery catheter to maintain high wedge

- **Aortic Insufficiency**
  - Usually rheumatic and associated with mitral disease
  - Generally well tolerated due to ↑ heart rate and decreased time for diastolic regurgitation
  - Complications usually due to concurrent mitral valve disease
  - SBE prophylaxis

D. Peripartum cardiomyopathy
- Describes women with heart failure with no readily apparent etiology – last month of pregnancy to 6 mo. postpartum
• Unlikely cardiomyopathy unique to pregnancy
• Often have superimposed preeclampsia, anemia or infection
• Diagnosis
  • Presents with signs and symptoms of heart failure
  • Symptoms – fatigue, dyspnea, orthopnea, cough, chest pain
  • Physical findings – elevated jugular venous pressure, rales, S3 gallop, edema
  • Hallmark finding cardiomegaly on chest x-ray
  • ECG nondiagnostic
  • Cardiac echo and Doppler flow studies confirm increased internal ventricular and atrial end-diastolic volumes and decreased ejection fraction
• Management
  • Treatment for heart failure
  • Use digitalis with caution – up to 50% have complex ventricular arrhythmias
  • Salt restriction, diuretics
  • Afterload reduction – hydralazine (may use captopril if postpartum)
  • Consider anticoagulation due to increased incidence of pulmonary embolism
• Future pregnancies 11-14% mortality if cardiac size normal in 6-12 mo., 40-80% with persistent cardiomegaly

E. Hypertrophic cardiomyopathy
• Idiopathic hypertrophic subaortic stenosis (IHSS)
• Commonly associated with pheochromocytoma, Friedreich ataxia, Turner syndrome, neurofibromatosis
• 1/2 inherited autosomal dominant with variable penetrance
• Idiopathic left ventricular hypertrophy, left ventricular outflow obstruction and mitral valve regurgitation
• Symptoms include dyspnea, anginal or atypical chest pain syncope
• Complex arrhythmias may develop leading to sudden death – most common reason
• Avoid hypotension and tachycardia
• β-blockers for angina, SVT, or β-blocker responsive arrhythmias
• SBE prophylaxis

F. Marfan syndrome
• Autosomal dominant with high degree of penetrance
• Caused by abnormal fibrillin gene on chromosome 15q
• Generalized weakness of connective tissue
• Progressive aortic dilatation can cause aortic valve insufficiency, infective endocarditis, mitral valve prolapse and mitral insufficiency
• Diagnosis
Aortic diastolic murmur
• Midsystolic click
• Echo shows aortic root dilation in 60% and mitral valve prolapse in 90%

• Aortic diameter < 40 mm = 5% mortality
• Aortic diameter > 40 mm = high risk of dissection
• Diameter < 40 mm propranolol used to decrease pulse rate; > 40 mm advise against pregnancy
• SBE prophylaxis

G. Ischemic heart disease
• Rare complication, 1/10,000
• Infarctions associated with PGE$_2$ suppositories, ergonovine for postpartum hemorrhage, bromocriptine
• Myocardial infarction during pregnancy has 30-35% mortality – worst prognosis in third trimester increased to 45%
• Timing of delivery – < 14 days, up to 50% mortality from MI
• Management
  • Strict limitation of physical activity
  • Usual medical treatment for signs and symptoms of coronary insufficiency or cardiac dysfunction

H. Arrhythmias, artificial valves and anticoagulants
• Arrhythmias – most not associated with organic heart disease, diagnosed with physical exam, ECG, Holter monitor
  • Bradyarrhythmias – including complete heart block
    - Usually have successful pregnancy outcomes
    - Syncope may occur during labor & delivery and require cardiac pacing
  • Tachyarrhythmias – fairly common
    - Consider underlying cardiac disease
    - Wolff-Parkinson-White syndrome may first appear during pregnancy
    - PSVT most commonly seen arrhythmia
    - Treatment
      - Vagal maneuvers
      - Digoxin, adenosine, calcium channel blockers
      - Cardioversion NOT contraindicated
      - Avoid fatigue, anxiety and stimulants (caffeine, nicotine)
  • Ventricular tachycardia
    - Most have structural heart disease
    - β-blocker therapy
  • Atrial flutter or atrial fibrillation
    - Look for underlying disease – thyrotoxicosis
    - Complications – thromboembolism
    - Treat with digitalis/quinidine
Artificial heart valves

- Prior valve replacement
  - Pregnancy complications
    - Thromboembolism
    - Hemorrhage from anticoagulation
    - Deterioration of cardiac function
    - Increased incidence of spontaneous abortion, stillbirth, low birth weight infants and malformed fetuses
  - Management
    - Full anticoagulation with heparin to prolong partial thromboplastin time (PTT) by 1.5-2.5 times baseline
    - Low molecular weight heparin may be used
    - Avoid warfarin (Coumadin)
    - Stop heparin prior to delivery (~ 4 hr. if IV, ~ 6-8 hr. if SQ)
    - Protamine sulfate may be given if anticoagulant is still effective
    - Restart anticoagulation 6 hr. after vaginal delivery, 24 hr. after cesarean delivery
    - Coumadin may be given postpartum, even if breastfeeding

- Porcine tissue valves
  - Anticoagulation not needed
  - Less durable than mechanical valves
  - Requires replacements

Anticoagulants

- Heparin side effects – bleeding 5-10%
  - Thrombocytopenia 5%
  - Osteoporosis
    - 2.2% symptomatic vertebral fractures
    - Found decrease in bone density by one-third

- Valve replacement during pregnancy
  - Most commonly mitral or aortic valve
  - Maternal mortality reported 2-10%
  - Fetal death rate 5-20%

Mitral valvotomy

- Following surgery functional NYHA class usually downgraded from Class II or IV to Class I (~ 81%)
- In series of 209 women, no maternal deaths
- 7% fetal deaths

XVI. Asthma

A. Introduction
• Asthma complicates 1-4% of pregnancies
• Status asthmaticus complicates 0.2% of pregnancies

B. Classification of asthma
• Extrinsic
  • IgE-mediated mast cell recognition of specific antigen
  • Known external allergens (dust, pollen, danders)
  • Elevated IgE in 50%
  • Other allergies common such as hay fever, eczema
  • Family history of multiple allergies common
• Intrinsic
  • No evidence of atopy (nonantigenic)
  • Bronchospasm induced in cold, exercise, pollution, infection or psychogenic
  • IgE normal or low
  • Other allergies uncommon
  • Family history of multiple allergies less common

C. Effects of pregnancy on asthma
• Pregnancy has no predictable effect on asthma: 1/3 improve, 1/3 worsen, 1/3 no change
• Women with severe asthma:
  • Are more likely to experience worsening disease than those with mild disease
  • In 60% of women, asthma behaves similarly with successive pregnancies
  • 10% will have exacerbation’s during labor and delivery
  • 18-fold increase risk of exacerbation following cesarean delivery compared to vaginal delivery

D. Effects of asthma on pregnancy
• Fetal
  • Preterm labor
  • Low birth weight
  • Fetal acidosis
  • Perinatal mortality
• Maternal
  • Preeclampsia
  • Gestational diabetes
  • Maternal deaths may be associated with status asthmaticus
  • Life-threatening complications include
    - Pneumothorax
    - Pneumomediastinum
    - Acute cor pulmonale
    - Cardiac arrhythmias
    - Respiratory arrest secondary to fatigue
  • Mortality rates exceed 40% when asthma requires intubation
E. Clinical course

- Acute bronchospasm leads to airway obstruction and decreased air flow
- Work of breathing increases, leading to tightness, wheezing, breathlessness
- Oxygenation is altered due to V/Q mismatch from airway narrowing
- Changes in pulmonary function are gradually reversed
- However, in the pregnant patient, with smaller functional residual capacity and increased effective shunt, is more susceptible to developing hypoxia and hypoxemia

F. Diagnosis of asthma

- Medical history
  - Recurrent episodic airway obstruction
  - Reversibility of obstruction
- Physical examination
  - Cough
  - Wheezing
  - Dyspnea or chest tightness
- Objective measures of lung function
  - FEV₁ (Forced expiratory volume in 1 second)
  - PEFR (Peak expiratory flow rate)

G. Clinical evaluation of asthma

- Subjective impression
- Clinical signs
  - Labored breathing
  - Tachycardia
  - Pulsus paradoxus
  - Prolonged expiration
  - Use of accessory muscles
- Signs of potentially fatal asthmatic attacks include:
  - Cyanosis
  - Altered level of consciousness
- Arterial blood gases
  - Provide direct analysis of oxygenation and acid-base status
  - PCO₂ > 35 mm Hg and pH < 7.35 is consistent with hyperventilation and CO₂ retention in a pregnant woman
- Pulmonary function testing
  - Most acceptable measure of severity of disease
  - Forced expiratory volume in one second (FEV₁), or peak expiratory flow rate (PEFR) are the most useful tests to measure airway obstruction
  - FEV₁ is single best measure for assessing severity
  - FEV₁ <1 liter, or <20% of predicted indicates severe disease
PEFR – greatest flow or velocity obtained during forced expiration beginning with fully-inflated lungs
- PEFR – not as sensitive a measurement of air flow obstruction; it underestimates degree of obstruction since less sensitive to decreased flows at low lung volume
- Using inexpensive portable equipment, PEFR does provide simple, quantitative, and reproducible measures of airway obstruction
- Predicted peak flow values for women are 380-550 liters/min.

- Pulse oximetry – maternal oxygen saturation must exceed 95% to be assured of adequate fetal oxygenation ($P_O_2 > 60$ mm Hg)
- Chest x-ray if clinical findings suggest pneumonia or pneumothorax

H. Clinical stages of asthma

<table>
<thead>
<tr>
<th>STAGE</th>
<th>$P_O_2$</th>
<th>$P_C_O_2$</th>
<th>pH</th>
<th>$FEV_1$* (% PREDICTED)</th>
<th>COMMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Normal</td>
<td>↓</td>
<td>↑</td>
<td>65-80</td>
<td>Mild respiratory alkalosis</td>
</tr>
<tr>
<td>II</td>
<td>↓</td>
<td>↓</td>
<td>↑</td>
<td>50-64</td>
<td>Respiratory alkalosis</td>
</tr>
<tr>
<td>III</td>
<td>↓</td>
<td>Normal</td>
<td>Normal</td>
<td>35-49</td>
<td>Danger zone</td>
</tr>
<tr>
<td>IV</td>
<td>↓</td>
<td>↑</td>
<td>↓</td>
<td>&lt; 35</td>
<td>Respiratory acidosis</td>
</tr>
</tbody>
</table>

*FEV$_1$ denotes forced expiratory volume (1 sec); from Barth and Hankins, 1991

I. Management of chronic asthma

- Maternal lung function
  - $FEV_1$/PEFR
  - Establish a personal best PEFR at time of good asthma control
  - Recommendations for changes in therapy may be based upon deviations from personal best
    - Increase maintenance medications if fall of $> 10\%$ from personal best
    - Acute intervention if fall of $20\%$
  - Fetal assessment
    - Early ultrasound
    - Serial scans for rate of growth
    - NST
    - Biophysical profiles
- Avoid or control asthma triggers
  - Environmental control
  - Immunotherapy
  - Physical activity
- Pharmacologic therapy
  - Step-care approach with the following goals
    - Normal (near normal) pulmonary function test
- Control symptoms – no nocturnal symptoms
- Normal activity, including exercise
- Prevent exacerbations
- Avoid adverse side effects from therapy
- Healthy infant

Bronchodilators – Beta-adrenergic agonists are first-line therapy
- bind to specific cell-surface receptors and activate adenylate cyclase which \( \uparrow \) CAMP (bronchial smooth-muscle relaxation)

Anti-inflammatory medications
- Inhaled corticosteroids preferred by many because of minimal side effects
- Cromolyn sodium stabilizes mast cell membranes. It has a preventive effect on asthma mediators and is used chronically
- Avoid narcotics (release histamine)
- Avoid prostaglandins
- Theophylline is a methylxanthine which acts as a bronchodilator
  - Aminophylline is a salt of theophylline and is used in a parenteral form
  - It was previously used in conjunction with \( \beta \)-agonists
  - Currently, it is being replaced by corticosteroids
  - No longer mainstay of therapy, but may be useful for out patient management for those who do not respond to \( \beta \)-agonists and corticosteroids

- Patient education
  - Partnership (woman/fetus/physician)
  - Education
  - Psychological support

J. Management of mild asthma
- Inhaled \( \beta \)-agonist prn
- More than 3 times/wk add anti-inflammatory therapy

K. Management of moderate or severe asthma
- Exacerbations frequent or chronic wheezing
- FEV\(_1\) and PEFR 60-80% of baseline
- Pharmacotherapy
  - Anti-inflammatory therapy
    - Inhaled corticosteroid – 400-800 µg/d
    - Cromolyn – 2 puffs/qid
  - Inhaled \( \beta \)-agonist prn/qid
  - SR-theophylline or oral \( \beta \)-agonist
  - Burst oral corticosteroid – 40 mg taper

L. Management of acute exacerbations
- Assess severity – PEFR/FEV\(_1\), symptoms
• Inhaled $\beta$-agonist 2-4 puffs q20 min x 3
  · Good response – PEFR 70-90% baseline
  · Incomplete response – PEFR 50-70% → emergency room
  · Poor response – PEFR > 50% → emergency room
• Inpatient treatment, if poor response
  · 23-hr stay
  · Intensive Care Unit
• Hydration will help clear pulmonary secretions
• Supplemental $O_2$ should be given
• Criteria for intubation
  · $PaCO_2 > 40$ mm Hg
  · $PaO_2 \leq 60$ mm Hg
  · $\leq 90\%$ oxygen saturation
  · Maternal exhaustion
• Corticosteroids should be given early in cases of severe acute asthma attacks– because their onset of action is several hours, steroids (either IV or aerosol) should be used along with $\beta$-agonists.
• Status asthmaticus – severe asthma not responding to 30-60 min. of intensive therapy
  · Admit to MICU
  · Early intubation
  · Fatigue, $CO_2$ retention, and hypoxemia are indications for intubation

M. Management of labor and delivery
• Continue medications
• Assess $FEV_1/PEFR$
  · Treat if symptomatic or $FEV_1/PEFR > 80\%$ baseline
  · Inhaled $\beta$-agonist, IV corticosteroids, oxygen
• Stress dose steroids should be considered for any woman who has received systemic steroid therapy in preceding 4 wk. (hydrocortisone 100 mg IV q 8 hr. for 24 hr.)
• Nonhistamine-releasing labor analgesia
  · Fentanyl or epidural analgesia
  · Avoid morphine or meperidine
• Vaginal delivery preferred
• Cesarean delivery
  · Epidural analgesia preferred
  · Avoid general anesthesia if possible since tracheal intubation may trigger bronchospasm. If it is necessary, use preoperative atropine and glycopyrrolate and halogenated anesthesia.
• For postpartum hemorrhage use PGE$_2$
  · Avoid 15-methyl prostaglandin F$_{2\alpha}$ and ergonovine because of associated bronchospasm
PGF\textsubscript{2α} may also cause O\textsubscript{2} desaturation

- MgSO\textsubscript{4} for tocolysis
- Avoid indomethacin

XVII. Surgical conditions during pregnancy

A. Questions to ask when presented with acute abdomen in pregnancy

- Early vs late pregnancy?
- Febrile vs non-febrile?
- Pregnancy complication or simply coincidentally occurring during pregnancy?

B. Early vs late pregnancy?

- In early pregnancy, consider ectopic pregnancy, adnexal disease such as ovarian torsion/ruptured cyst in addition to more traditional causes of acute abdomen such as appendicitis, cholecystitis, perforated/ischemic bowel
- In late pregnancy, consider all (except ectopic, which is rare with intrauterine pregnancy) in addition to pregnancy complication

C. Febrile vs non-febrile?

- If febrile, consider infectious etiology (appendicitic, cholecystitis)
- If afebrile, consider other etiologies

  **PID RARE WITH ESTABLISHED PREGNANCY OF ANY GESTATIONAL AGE**

D. Pregnancy complication vs problem coincident with pregnancy?

- In late pregnancy, consider abruption placenta, uterine rupture, labor as causes of abdominal pain that mimic acute abdomen

E. Special considerations when evaluating pregnancy

- Delayed GI motility
- Change in location of appendix from McBurney’s point
- Decreased ability to “wall off” abscess due to uterus
- Uterus in mid-abdomen prevents standard exam of abdomen
- Fetus precludes certain drugs being used
- Risk of preterm labor when opening abdomen during pregnancy

F. Clinical evaluation of acute abdomen during pregnancy

- Early pregnancy: ultrasound to document intrauterine pregnancy; may consider laparoscopy
- Early and late pregnancy: CBC, UA, LFTs, fetal monitor; may consider exploratory laparotomy with concomitant tocolytics to reduce preterm labor symptoms that frequently accompany surgery during pregnancy

**Reference**
