Preterm Labor and Preterm Prelabor Rupture of Membranes

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Objectives

- Identify the risk factors and causes for PTL and PPROM
- Describe signs and symptoms of PTL and PPROM
- Describe initial management of PTL and PPROM
- List indications & contraindications of medications used in PTL
- Identify adverse outcomes associated with Preterm Delivery
- Counsel patient regarding risk reduction for PTB
Preterm Labor: Definition

- Uterine contractions WITH any of the following:
  - Cervical “change”
  - > or equal to 2cm dilation
  - > or equal to 80% effacement

- Preterm delivery <37 weeks
Epidemiology

- ~12% Incidence, 2% <32 weeks
- Preterm Birth accounts for:
  - 70% neonatal deaths
  - 36% infant deaths
  - 25-50% of long-term neurologic impairment
- Annual cost (2006) $26.2 billion = $51,000/infant
- No improvement with physician intervention 😞
Preterm Birth: Infant Mortality

![Graph showing the relationship between gestation at birth and infant mortality.](image-url)
Preterm Birth: Infant Morbidity

![Graph showing the percentage of infants with various morbidities at different gestational weeks.](image-url)
Risk Factors for Preterm Birth

- Non-modifiable
  - Prior PTB
  - Black
  - Age <18 or >40
  - Poor nutrition
  - Low SES
  - Uterine anomaly/fibroid
  - Cervical injury
  - Premature cervical dilation
  - Over-distended uterus

- Modifiable/Other
  - Cigarette smoking
  - Substance Abuse
  - Absent PNC
  - Short Pregnancy Interval
  - Anemia
  - Bacteriuria/UTI
  - Cervicitis
  - Periodontal disease
  - Depression and anxiety
  - Placental abruption
  - Vaginal bleeding
# Preterm Birth: Recurrence

<table>
<thead>
<tr>
<th>First Birth</th>
<th>Second Birth</th>
<th>Subsequent PTB Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Term</td>
<td>Term</td>
<td>4.4%</td>
</tr>
<tr>
<td>Preterm</td>
<td>Term</td>
<td>17.2%</td>
</tr>
<tr>
<td>Term</td>
<td>Term</td>
<td>2.6%</td>
</tr>
<tr>
<td>Preterm</td>
<td>Term</td>
<td>5.7%</td>
</tr>
<tr>
<td>Term</td>
<td>Preterm</td>
<td>11.1%</td>
</tr>
<tr>
<td>Preterm</td>
<td>Preterm</td>
<td>28.4%</td>
</tr>
</tbody>
</table>

- Prior PTB @ 23-27 weeks: 27%
- Prior PPROM: 13.5%
Pathogenesis

- 80% of preterm births are spontaneous
  - 50% Preterm Labor
  - 30% PPROM

- Pathogenic Process
  - Activation of the maternal or fetal hypothalamic pituitary axis
  - Infection
  - Decidual hemorrhage
  - Pathologic Uterine Distention
Pathogenesis: Inflammation

- **Clinical/subclinical chorioamnionitis**
  - Up to 50% of preterm birth < 30 wks GA

- **Proinflammatory mediators**
  - Maternal/fetal inflammatory response
  - Activated neutrophils/macrophages
  - TNF alpha, interleukins (6)

- **Bacteria**
  - Degradation of fetal membranes
  - Prostaglandin synthesis
Measures to Predict Preterm Birth

- History: Current and historical risk factors
- Mechanical: Uterine Contractions
- Biochemical: Fetal Fibronectin
- Ultrasound: Cervical Length
History of Preterm Birth <34 weeks

- May Consider Serial Transvaginal Cervical Length Screening, Q 2 weeks from 16-23 weeks.
  - If 25mm to 29mm increase to weekly screening
  - If <25mm ➔ cerclage

- If no history of PTB, and asymptomatic, but found to incidentally have a very short cervical length less than or equal to 20mm before 24 weeks ➔ Vaginal Progesterone
Mechanical: Preterm Contractions

- 30% of preterm labor resolves spontaneously
- 50% of patients hospitalized for PTL give birth at term.
- <10% of patients with clinical dx of PTL give birth within 7 days.

CONTRAINDICATIONS TO TOCOLYSIS

- IUFD
- Lethal fetal anomaly
- NRFHTs
- Severe preeclampsia or eclampsia
- Maternal bleeding with hemodynamic instability
- Chorioamnionitis
- PPROM*
- Maternal contraindications
Biochemical: Fetal Fibronectin

- Glycoprotein in amnion, decidua, cytotrophoblast
- Increased levels d/t breakdown of chorionic-decidual surface
- Inflammation, shear, movement

Contraindications to collecting fFN:
- <24 or >34 weeks
- ROM
- >/=3cm dilation
- Active vaginal bleeding
- Exam or sexual intercourse in last 24h

Sensitivity (all): 93%, PPV 29%, NPV 99%
Ultrasound: Cervical Length
Evaluating a ‘R/O PTL’

- PROMPT EVALUATION
- EFM/TOCO
- Where is the placenta? If you don’t know: abdominal u/s first
- UA and culture
- Speculum exam: determine status of cervix
  - Collect cultures: GC/CT, FFN
  - Rectovaginal Swab for GBS
  - Wet Prep/KOH, Ferning
- SVE
- US exam: Assess GA, CL, AFI, Presentation, Placentation
Antenatal steroids are the most beneficial intervention of all to improve neonatal outcomes

- 23-34 weeks if risk of delivery is <7d
- Repeat course if prior course was >/= 7 days before and still at risk for PTB <34 weeks

- Betamethasone: 12mg IM q24hr x2 doses
- Dexamethasone: 6mg IM q 12hr x4 doses
Management: Magnesium & Tocolysis

- **Magnesium sulfate:**
  - reduces the occurrence of cerebral palsy when given (RR, 0.71; 95% CI 0.55-0.91) prior to 32 weeks

- **Tocolysis:**
  - May be given to allow for the administration of steroids (48h)
  - Longer administration has no impact on neonatal outcomes
<table>
<thead>
<tr>
<th>Drug</th>
<th>Mechanism</th>
<th>Efficacy</th>
<th>Side Effects</th>
<th>Contraindications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beta adrenergic receptor agonist (Terbutaline*)</td>
<td>Interferes w/ myosin light chain kinase Inhibits actin myosin interaction</td>
<td>No change in perinatal outcome</td>
<td>Tachycardia, palpitations, hypotension, SOB, pulmonary edema, hyperglycemia, Fetal tachycardia</td>
<td>Maternal cardiac disease, uncontrolled diabetes</td>
</tr>
<tr>
<td>Magnesium Sulfate</td>
<td>Competes with Calcium at plasma membrane</td>
<td>Unproven</td>
<td>Diaphoresis, flushing, pulmonary edema</td>
<td>Myasthenia gravis, renal failure</td>
</tr>
<tr>
<td>Ca Channel Blocker (Nifedipine)</td>
<td>Directly block influx of Ca thru cell membrane</td>
<td>Unproven</td>
<td>Nausea, flushing, HA, palpitations</td>
<td>Caution: LV dysfunction, CHF</td>
</tr>
<tr>
<td>Cyclooxygenase Inhibitors/NSAIDS (Indomethacin)</td>
<td>Decrease prostaglandin production</td>
<td>Unproven</td>
<td>Nausea, GI reflux, spasm fetal DA, oligohydramnios, necrotizing enterocolitis in newborn</td>
<td>Platelet or hepatic dysfunction, GI ulcer Renal dysfunction, asthma</td>
</tr>
</tbody>
</table>
Management: Antibiotics

- Antibiotics should not be used to prolong gestation or improve neonatal outcomes in women with PTL and intact membranes.

- GBS prophylaxis should be used for carriers or if patient is GBS unscreened and has risk factors.
  - Prior infant with invasive GBS disease or prior pregnancy with +GBS
  - GBS bacteriuria this pregnancy
  - **Delivery <37wks**
  - ROM greater or equal to 18hrs
  - Intrapartum temperature greater or equal to 100.4 F
Preventative Measures

- Progesterone Supplementation
  - Women with a prior singleton spontaneous PTB
  - Start at 16 weeks gestation
  - 17 alpha OH Progesterone (Makena): 250mg IM q week
  - Vaginal Progesterone 90-200mg daily

- 17-OH-P: Reduces Risk of Recurrent Preterm birth
  - <37 wks 36% vs 55%
  - <35 wks 21% vs 31%
  - <32 wks 11% vs 20%
Take Home Points: PTL

- Defined by “regular” uterine contractions, with cervical “change” or ≥ 2 cm dilation or ≥ 80% effacement, occurring before 37 weeks

- There are numerous risk factors – both modifiable and non-modifiable. Counsel patients regarding ways to reduce their modifiable risk factors

- Clinical assessment of risk includes consideration and evaluation of history, cervical length and fetal fibronectin

- There are a variety of tocolytic drugs available, though most have unproven efficacy

- Antenatal steroids are recommended for: Preterm labor 24 – 34 weeks
Preterm Prelabor Rupture of Membranes (PPROM)

- Prelabor rupture of membranes (PROM)
  - Rupture of the chorioamnionic membrane prior to the onset of labor at any stage of gestation

- Preterm prelabor rupture of membranes (PPROM)
  - PROM <37 wks
Incidence of PROM

- PROM – 12% of all pregnancies
- PROM – 8% term pregnancies
- PPROM – 30% of preterm deliveries
Evaluation: R/O PPROM

- History
  - “Gush” of fluid
  - Steady leakage of small amounts of fluid

- Physical
  - Sterile vaginal speculum exam
    - Minimize digital examination of cervix, regardless of gestational age, to avoid risk of ascending infection/amnionitis
    - Assess cervical dilation and length (visually if possible)
    - Obtain cervical cultures (Gonorrhea, Chlamydia)
    - Obtain amniotic fluid samples
Diagnosis

- **Speculum Examination**
  - Pooling of amniotic fluid in posterior vaginal fornix
  - Fluid per cervical os

- **Nitrazine test**
  - Fluid from vaginal exam placed on strip of nitrazine paper
  - Paper turns blue in presence of alkaline (pH > 7.1) amniotic fluid

- **Fern test**
  - Fluid from vaginal exam placed on slide and allowed to dry
  - Amniotic fluid narrow fern vs. cervical mucus broad fern
Testing pitfalls

- False positive Nitrazine test
  - Alkaline urine
  - Semen (recent coitus)
  - Cervical mucus
  - Blood contamination
  - Vaginitis (e.g. Trichomonas)

- False-Negative Nitrazine test
  - Remote PROM with no residual fluid
  - Minimal amniotic leakage
Diagnosis

- Ultrasound
  - Assess amniotic fluid level and compatibility with PROM
- Indigo-carmine Amnioinfusion
  - Ultrasound guided indigo carmine dye amnioinfusion ("Blue tap")
  - Observe for passage of blue fluid from vagina
PPROM Risk Factors

- Risk Factors:
  - Prior PROM or PPROM
  - Prior preterm delivery
  - Multiple gestation
  - Polyhydramnios
  - Cervical Insufficiency
  - Vaginal/Cervical Infection
    - Gonorrhea, Chlamydia, GBS, S. Aureus
  - Antepartum bleeding (threatened abortion)
  - Smoking
  - Poor nutrition
Management of PPROM <23 weeks

- Patient counseling

<table>
<thead>
<tr>
<th>Gestational Age (In Completed Weeks)</th>
<th>Death Before NICU Discharge</th>
<th>Death</th>
<th>Death/ Profound Neurodevelopmental Impairment</th>
<th>Death/Moderate to Severe Neurodevelopmental Impairment</th>
</tr>
</thead>
<tbody>
<tr>
<td>22 Weeks</td>
<td>95%</td>
<td>95%</td>
<td>98%</td>
<td>99%</td>
</tr>
<tr>
<td>23 Weeks</td>
<td>74%</td>
<td>74%</td>
<td>84%</td>
<td>91%</td>
</tr>
<tr>
<td>24 Weeks</td>
<td>44%</td>
<td>44%</td>
<td>57%</td>
<td>72%</td>
</tr>
<tr>
<td>25 Weeks</td>
<td>24%</td>
<td>25%</td>
<td>38%</td>
<td>54%</td>
</tr>
</tbody>
</table>

- Expectant management vs. induction of labor
- GBS prophylaxis NOT recommended
- Antibiotics
  - Incomplete data
- Corticosteroids NOT recommended
Complications of Prolonged PPROM

- Fetal complications of prolonged PPROM
  - Pulmonary hypoplasia
  - Skeletal malformations
  - Fetal growth restriction
  - IUFD
- Maternal complications of prolonged PPROM
  - Chorioamnionitis

http://www.nichd.nih.gov/about/org/cdbpm/pp/prog_epbo/dataShow.cfm
Management of PPROM 23-33 weeks

- Expectant management
  - Deliver at 34 wks
  - Unless documented fetal lung maturity
- GBS prophylaxis
- Latency Antibiotics
- Corticosteroids
- Tocolytics
  - No consensus
- Magnesium Sulfate
Management of PPROM $\geq 34$ weeks

- Deliver: Induction of labor
- GBS prophylaxis
Rationale for Interventions

- **Antibiotics**
  - Prolong latency period
  - Prophylaxis of GBS in neonate
  - Prevention of maternal chorioamnionitis and neonatal sepsis

- **Corticosteroids**
  - Enhance fetal lung maturity
  - Decrease risk of RDS, IVH, and necrotizing enterocolitis

- **Tocolytics**
  - Delay delivery to allow administration of corticosteroids
  - Controversial, randomized trials have shown no pregnancy prolongation
Interventions

- **Antibiotics**
  - Ampicillin 2g q6h and Erythromycin 250mg q6h x48h
  - Amoxicillin 250mg q8h and erythromycin 333mg q8h x5d

- **Corticosteroids**
  - Betamethasone 12 mg IM q24 x 2
  - Dexamethasone 6 mg IM q12 x 4
  - *No consensus on whether to give 32-34 weeks

- **Magnesium Sulfate**
  - 4g bolus then 2g/h if <32 weeks

- **Tocolytics**
  - Indocin if <32 weeks 100mg PO x1, then 25mg PO q4h
  - Nifedipine 10 mg po q20min x 3, then q6 x 48 h, though
Surveillance

- Maternal: Monitor for signs of infection
  - Temperature
  - Maternal heart rate
  - Fetal heart rate
  - Uterine tenderness
  - Contractions

- Fetal: Monitor for fetal well-being
  - Kick counts
  - Nonstress tests (NSTs)
  - Biophysical profile (BPP)
Deliver if:

- Intrauterine infection
- Abruptio placenta
- Repetitive fetal heart rate decelerations
- Cord prolapse
Risks of Expectant Management

- **Maternal**
  - Increase in chorioamnionitis
  - Increase in Cesarean delivery
  - Spontaneous labor in ~ 90% within 48 hr ROM
  - Increased risk of placental abruption

- **Fetal**
  - Increase in RDS
  - Increase in intraventricular hemorrhage
  - Increase in neonatal sepsis and subsequent cerebral palsy
  - Increase in perinatal mortality
  - Increase in cord prolapse
Take Home Points: PPROM

- Preterm premature rupture of membranes refers to rupture of fetal membranes prior to labor in pregnancies < 37 weeks.

- A history of PPROM or PROM, genital tract infection, antepartum bleeding, and smoking are risk factors for PPROM and PROM.

- A clinical history suggestive of PPROM or PROM should be confirmed with visual inspection and laboratory tests including fering and nitrazine paper.

- Management of PPROM at < 24 wks includes a discussion with the family reviewing the maternal risks against the fetal risks of significant morbidity and mortality during expectant management.

- For women with PPROM or PROM in whom intrauterine infection, abruptio placenta, repetitive fetal heart rate decelerations, or a high risk of cord prolapse is present, immediate delivery is recommended.

- Counseling after the delivery for the recurrence risk of PROM should occur, and modifiable risk factors addressed