PRETERM LABOR

Elyse Watkins, DHSc, PA-C, DFAAPA
Preterm labor is defined as the presence of uterine contractions of sufficient frequency and intensity to effect progressive effacement and dilation of the cervix prior to term gestation.

Preterm birth is defined as birth between 20 0/7 weeks of gestation and 36 6/7 weeks of gestation.
Epidemiology

- ~30% of preterm labor spontaneously resolves
- ~50% of women hospitalized for preterm labor actually give birth at term

Preterm births account for:
- Approximately 70% of neonatal deaths
- 36% of infant deaths
- 25–50% of cases of long-term neurologic impairment in children
Risk Factors

- Abruptio
- Uterine overdistention: multiple gestation, polyhydramnios
- Cervical incompetence: trauma, cone biopsy
- Shortened cervix (< 25 mm before 28 weeks' gestation)
- Uterine anomalies: müllerian duct abnormalities, fibroid uterus
- Cervical inflammation: BV, trichomonas, GC, CT
- Infection: UTI, intrauterine infections, others
- Uteroplacental insufficiency (eg, hypertension, IDDM, drug abuse, smoking, alcohol consumption)
  - Heroin, tobacco, and cocaine ↑
- Periodontal disease
- Hx of spontaneous preterm delivery: 1.5 to 2 times more likely to have a subsequent preterm delivery
- Short pregnancy interval (< 18 months between pregnancies)
Midline sagittal image of the uterine cervix at 22 weeks of gestation obtained with an 8 MHz transvaginal ultrasound transducer.
Diagnosis

■ Based on clinical criteria:
  – regular uterine contractions accompanied by a change in cervical dilation, effacement, or both
  – or initial presentation with regular contractions and cervical dilation of at least 2 cm.

■ Less than 10% of women with the clinical diagnosis of preterm labor actually give birth within 7 days of presentation
Singleton deliveries by race and preterm status, all included states

<table>
<thead>
<tr>
<th></th>
<th>Black women</th>
<th></th>
<th>Non-Black women</th>
<th></th>
<th>Overall</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>Preterm deliveries</td>
<td>54,040</td>
<td>11.0%</td>
<td>179,206</td>
<td>7.3%</td>
<td>233,246</td>
<td>7.9%</td>
</tr>
<tr>
<td>Term deliveries</td>
<td>438,264</td>
<td>89.0%</td>
<td>2,286,524</td>
<td>92.7%</td>
<td>2,724,788</td>
<td>92.1%</td>
</tr>
<tr>
<td>Total</td>
<td>492,304</td>
<td>100.0%</td>
<td>2,465,730</td>
<td>100.0%</td>
<td>2,958,034</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

Table includes singleton live births that had a gestational age of at least 20 weeks, took place in 2016, had complete data for all study variables, occurred in a hospital, were paid for by either Medicaid or a private insurer, and occurred in one of the 35 states included in this analysis.
*Categories based on state odds ratios for preterm delivery among Black women (presented in Table 3).
Patient Assessment

- Must verify dates
- Must rule out ROM
- Evaluate for GBS status, UTI, BV, and STIs (trichomoniasis, gonorrhea, chlamydia)
Predictive tools: Cervical length

- A “short cervical length” (CL) assessment by transvaginal ultrasound between 16 and 24 weeks of gestation is a reasonably accurate predictor of spontaneous preterm birth (SPTB).

- Risk of SPTB is inversely proportional to the CL; those with the shortest CL have the highest risk of SPTB, regardless of reproductive history.
Predictive Tools: Fetal Fibronectin

- A high level (>50 ng/mL) of FFN in the cervicovaginal secretions ≥ 22 weeks increases the risk of spontaneous preterm birth.
- Screening for FFN has an “excellent NPVe for predicting the absence of spontaneous preterm birth at 48 hours and 7 days.”
- The PPV of a positive fetal fibronectin test result or a short cervix alone is poor and should not be used exclusively to direct management.
- FFN seems to be most helpful for a 'borderline' CL of 20 to 29 mm.
- CL < 20 mm or an intermediate CL with a positive FFN screen should be given corticosteroids.
Treatment

- Historically, nonpharmacologic treatments included bed rest, abstention from intercourse and orgasm, and hydration.
- Pharmacologic interventions to prolong pregnancy have included tocolytic drugs, progesterone, and antibiotics.
Vaginal Progesterone

- **Current recommendations:**
  - Vaginal progesterone in women with a shortened cervix and no history of preterm delivery
  - Progesterone supplementation regardless of cervical length in women with a history of spontaneous preterm delivery

- Associated with a **significant reduction in the risk of preterm birth** <33 weeks of gestation (high-quality evidence).

- **Significantly decreased the risk of preterm birth** <36, <35, <34, <32, <30, and <28 weeks of gestation; **spontaneous preterm birth** <33 and <34 weeks of gestation; **respiratory distress syndrome**; composite neonatal morbidity and mortality; **low birthweight** <1500 and <2500 g; and **admission to the NICU** (high-quality evidence for all)

## Vaginal Progesterone

<table>
<thead>
<tr>
<th>Natural micronized progesterone</th>
<th>Vaginal suppository</th>
<th>100, 200, 400mg</th>
<th>Daily</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaginal gel</td>
<td></td>
<td>90mg</td>
<td>Daily</td>
</tr>
</tbody>
</table>
Progesterone

- **PROLONG** (Progestin's Role in Optimizing Neonatal Gestation) trial:
  - a multicenter, multinational, placebo-controlled, randomized clinical trial (RCT) designed to assess the safety and efficacy of Makena (hydroxyprogesterone caproate injection, 250 mg/mL)

- Difference in population when analyzing Meis et al. vs PROLONG
  - Higher rate of black women: 59% vs 7%
  - Smoking (tobacco): >20% vs 8%
  - >1 prior PTB: 32% vs 12%
  - Additional PTB risk factors aside from prior history: 91% vs 48%

- On October 29, 2019, the FDA recommended the drug be withdrawn from the market

Progesterone

- SMFM: it is reasonable for providers to use 17-OHPC in women with a profile more representative of the very high-risk population.

- ACOG: not changing our clinical recommendations at this time and continues to recommend offering hydroxyprogesterone caproate as outlined in Practice Bulletin # 130.
Tocolytics

- Generally is effective for up to 48 hours.
- Only women with fetuses that would benefit from a 48-hour delay in delivery should receive tocolytic treatment.
- The upper limit has been 34 weeks’ gestation
- **No evidence exists** to support the use of prophylactic tocolytic therapy, home uterine activity monitoring, cerclage, or narcotics to prevent preterm delivery in women with contractions **but no cervical change**
- “No evidence exists that it has any direct favorable effect on neonatal outcomes or that any prolongation of pregnancy afforded by tocolytics actually translates into statistically significant neonatal benefit.”
Corticosteroids

A single course of corticosteroids is recommended for pregnant women between 24 weeks and 34 weeks of gestation who are:
- At risk of delivery within 7 days
- With multiple gestations or ROM

May be considered at 23 wks in women with significant risk factors regardless of membrane status
Corticosteroids

- Using corticosteroids when imminent preterm birth exists is strongly associated with decreased neonatal morbidity and mortality
- Results in significantly lower severity, frequency, or both of respiratory distress syndrome, intracranial hemorrhage, necrotizing enterocolitis, and death
Corticosteroids

- Dosage:
  - Two 12-mg doses of IM betamethasone 24 hours apart
  - Four 6-mg doses of IM dexamethasone every 12 hours
Magnesium sulfate

- Association between prenatal exposure to magnesium sulfate and less frequent occurrence of subsequent neurologic morbidities
- Predelivery administration reduces the occurrence of cerebral palsy when given with neuroprotective intent
- Reduces the severity and risk of cerebral palsy in surviving infants if administered when birth is anticipated before 32 wks’ gestation.
- Data support the use of a minimal dose (4 g loading dose ± 1 g/h maintenance dose over 12 h) in women at risk of preterm delivery ≤32 wks’ gestation
Magnesium sulfate

- Vital signs, oxygen saturation, deep tendon reflexes, and level of consciousness should be monitored.
- Signs of toxicity: visual changes, somnolence, flushing, muscle paralysis, loss of patellar reflexes, pulmonary edema.
Cerclage

- Associated with a decrease in preterm delivery and in perinatal death when used in women with a prior preterm delivery and a cervical length of 25 mm or less
- Placed between 12 and 18 wks’ gestation
- Not recommended for multifetal gestations
- Pessary?
Antibiotics

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

- National Institute of Child Health and Human Development - Maternal Fetal Medicine Units (NICHD-MFMU) study of PROM and the ORACLE trial
  - Looked at abx in PPROM (24 – 37 wks’ gestation)
  - Amp vs erythro vs amox-clavulanic acid
  - No differences between the various abx BUT slightly increased incidence of nectrotizing enterocolitis with amox/clav acid
Areas of interest

- Endocannabinoids/endovanilloid (EC/EV) system and inflammation are recognized as key regulators of cell-signaling pathways in female reproduction
  - marked increase of CB1, anandamide, and inflammatory cytokines, mainly TNF-α, together with TRPV1 down-regulation in term delivery group, compared to preterm groups
Areas of interest

- Complement components C1q and C5b-9
  - deposited on fetal membranes and release inflammatory mediators that contribute to uterine contractions, cervical ripening, cell chemotaxis, metalloproteinases production, membrane awaking and rupture, and participates as a co-adjuvant in the onset and progress of labor.
Areas of interest

- Lactobacillus species:
  - protector in the vaginal microbiome
  - demonstrated to be a protector of spontaneous preterm outcome whereas the presence of pathogenic species, such as Prevotella spp., is a risk factor for spontaneous preterm delivery.

- Lactobacillus gasseri/L. johnsonii, L. crispatus/L. acidophilus, L. iners/R. solanacearum and B. longum/B. breve may be associated with decreased risk of early preterm birth.
Areas of interest

- High levels of AFP and b-hCG but low levels of uE3 were significantly associated with higher rates of preterm, early preterm and very early preterm delivery.
Areas of interest

- Placental alpha microglobulin-1 is a better predictor of imminent spontaneous preterm birth when compared with phosphorylated insulin-like growth factor-binding protein-1 alone or in combination with cervical length measurement.

- In patients with cervical length of 15-30 mm, the placental alpha microglobulin-1 test is a significantly better predictor of imminent spontaneous preterm birth within 7 days of testing than is phosphorylated insulin-like growth factor-binding protein-1.
Areas of interest

References

- ACOG Practice Bulletin Number 171, October 2016
The End