Welcome to the Pregnancy Medical Home “First Tuesdays” Webinar: Prevention of Preterm Birth: Progesterone Therapy

Webinar will begin at 7:30am
Connect to audio by computer
Submit any questions through chat

Funding for this project is provided in part by The Duke Endowment
PMH Care Pathways

CCNC network OB champions collaborate to create evidence-based clinical guidance for maternity care providers, in order to promote best practices and improve quality and outcomes.

Currently available PMH Care Pathways:

- Hypertensive Disorders of Pregnancy
- Induction of Labor in Nulliparous Patients
- Perinatal Tobacco Use
- Postpartum Care and the Transition to Well Woman Care
- Progesterone Treatment and Cervical Length Screening
- Substance Use in Pregnancy

https://www.communitycarenc.org/population-management/pregnancy-home/pmh-pathways/
Prevention of Preterm Birth: Progesterone Therapy
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Maternal-Fetal Medicine Specialist, Cape Fear Valley Perinatology
Medical Director of Obstetrics, Cape Fear Valley Medical Center

Funding for this project is provided in part by The Duke Endowment
Learning Objectives

By the end of this session, participants will be able to:

- Recognize benefits of screening patients for progesterone use
- Identify indications for 17P
- Identify indications for vaginal progesterone
- Identify indications for cerclage for short cervix
- Recognize controversial management areas for multiple gestations

17P = 17α-hydroxyprogesterone caproate

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Background

Preterm Birth: Why worry?

1) Very common (~ 450,000 infants/yr)
2) Very expensive (~ $26 billion/yr)*
3) #1 cause of infant deaths
4) Intervention can reduce the risk

2014 March of Dimes Report Card

North Carolina

<table>
<thead>
<tr>
<th>Year</th>
<th>Preterm (&lt; 37 weeks)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2006</td>
<td>13.6%</td>
</tr>
<tr>
<td>2010</td>
<td>12.7%</td>
</tr>
<tr>
<td>2014</td>
<td>12.0%</td>
</tr>
<tr>
<td>2020 Goal</td>
<td>9.6%</td>
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</tbody>
</table>
Preterm Birth: Etiology

- Preterm labor/PROM: 70%
- Medical/obstetrical indications: 30%

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### Recurrence Risks for Spontaneous Preterm Birth

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Risk of SPTB in next pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>2nd pregnancy; 1st at term</td>
<td>9%</td>
</tr>
<tr>
<td>2nd pregnancy; 1st SPTB</td>
<td>22%</td>
</tr>
<tr>
<td>3rd pregnancy; 2 Prior SPTBs</td>
<td>42%</td>
</tr>
<tr>
<td>both &lt; 32 weeks</td>
<td>57%</td>
</tr>
<tr>
<td>3rd pregnancy; 2 Term births</td>
<td>5%</td>
</tr>
</tbody>
</table>

Mercer (1999)
McManemy (2007)
Progesterone Therapy

Two different preparations with two different indications

17P:
- prior spontaneous preterm birth

Vaginal progesterone:
- incidentally detected short cervix (ultrasound)
17α-hydroxyprogesterone (17P)
Evidence supporting 17P

NICHD randomized controlled trial (2003)

Eligible participants:
Prior spontaneous preterm birth 20° – 36°
Enrolled at 16-20 weeks
Weekly 17P (250 mg) vs. placebo until 36 weeks

Meis (2003)
### Evidence for 17P

<table>
<thead>
<tr>
<th>Gestation value</th>
<th>Placebo</th>
<th>17P</th>
<th>RR</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 37 weeks</td>
<td>55%</td>
<td>36%</td>
<td>0.66</td>
<td>0.001</td>
</tr>
<tr>
<td>&lt; 35 weeks</td>
<td>31%</td>
<td>21%</td>
<td>0.67</td>
<td>0.017</td>
</tr>
<tr>
<td>&lt; 32 weeks</td>
<td>20%</td>
<td>11%</td>
<td>0.58</td>
<td>0.018</td>
</tr>
</tbody>
</table>

Approximately 33% reduction in preterm births

Meis (2003)
Initial recommendation (2008)

Progestrone (17P) supplementation should be offered to women with a current singleton pregnancy and a prior spontaneous singleton preterm birth (start at 16-24 weeks)

Use in multiple gestations is not recommended

NC Pregnancy Medical Home (2011) requires PMH providers to offer and provide 17P to eligible patients
17P Candidates and use

- Take a good history. Not indicated, if prior preterm birth was secondary to a medical or obstetrical indication.

- Previous singleton spontaneous preterm birth < 37 weeks

- Begin at 16-20 weeks and continue until 36 weeks
  - Start by 24 weeks at latest*
  - 250 mg IM weekly

- If dose is missed, resume therapy as soon as possible

*NC Medicaid will reimburse for 17p treatment for any patient with a history of spontaneous preterm birth regardless of weeks of gestation at initiation of therapy.
Management dilemmas

- Prior SPTB of a twin gestation and now has a singleton
  - High-risk Ob consult
  - Consider 17P, if prior birth was “early” (i.e. < 30 weeks)

- Should 17P be continued, if a cerclage is done for a short cervix?
  - Yes

- Should 17P be used following tocolysis?
  - No, unless she was previously receiving it prior to tocolysis

- Should it be used in patients with risk factors for preterm birth, but no prior SPTB (multiples, uterine anomaly, + fFN, etc.)?
  - No

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Vaginal Progesterone
Evidence for Vaginal Progesterone

Randomized controlled trial:
- Asymptomatic women with cervix < 15 mm (20-25 wks)
- Vaginal progesterone (200 mg daily) vs. placebo
- 24-34 weeks

Delivery < 34 weeks

<table>
<thead>
<tr>
<th></th>
<th>Progesterone:</th>
<th>Placebo:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>19%</td>
<td>34%</td>
</tr>
<tr>
<td>Reduction</td>
<td>(44% reduction)</td>
<td></td>
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</table>

Fonseca (2007)

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Assess cervical length by transabdominal ultrasound at time of fetal anatomic survey. If cervix appears short (i.e. < 25 mm), perform transvaginal ultrasound

- (transabdominal cervical length for low-risk patients only)

Consider vaginal progesterone for asymptomatic women with a singleton gestation and no prior spontaneous preterm birth who have an incidental finding of short cervix (< 20 mm) before 24 weeks
Progesterone Formulations

17P
- Makena®
- Compounded

Vaginal progesterone
- Prometrium® 200 mg (oral tablets, but use per vagina)
- Crinone® 90mg gel

All of these preparations are covered by NC Medicaid; for more information or technical assistance, contact your local CCNC OB team.
Cerclage
Prior SPTB and short cervix

Meta-analysis (5 studies)
- singleton gestation
- prior SPTB
- current cervical length < 25 mm before 24 weeks
- randomized to cerclage vs. no cerclage

Delivery < 35 weeks
- cerclage: 28.4% RR: 0.70 (30% reduction)
- no cerclage: 41.3%

Berghella (2011)

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Multiple Gestation
Twins and short cervix

- Cerclage
  - not recommended
  - associated with 2-fold increase in preterm births*

- Vaginal progesterone
  - no effect on preterm delivery rate
  - ACOG: not recommended
  - some experts recommend**:  
    ~ 50% decreased risk of adverse perinatal outcome  
    (RDS, IVH, NEC, sepsis, or neonatal death)

*Berghella (2005)
**Romero (2012)
Summary
Recommendations:

Singleton gestation

Prior spontaneous preterm birth < 37 weeks
- consider high risk pregnancy consultation
- weekly 17P from 16-36 weeks

Prior spontaneous preterm birth < 32 weeks
- obtain high-risk pregnancy consultation
- weekly 17P from 16-36 weeks
- transvaginal cervical length every 2 weeks from 15-23 weeks
- if cervix is 25-29 mm, assess weekly
  - consider cerclage, if cervix is < 25 mm
Recommendations: Singleton gestation

No prior spontaneous preterm births

- transabdominal cervical length at anatomy scan (18-24 wks)
- if cervix is < 30 mm, perform transvaginal ultrasound
- if cervix is < 25 mm by transvaginal ultrasound:
  - vaginal progesterone
    - 200mg tablets (Prometrium®) nightly
    - 90mg gel (Crinone®) nightly
Recommendations:
Multiple gestation

Prior SPTB:
- consider 17P

Short cervix:
- no cerclage (doubles risk for preterm delivery)
- consider vaginal progesterone

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<table>
<thead>
<tr>
<th>Current pregnancy</th>
<th>Past SPTB</th>
<th>Recommendation</th>
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</thead>
<tbody>
<tr>
<td>Singleton</td>
<td>Singleton</td>
<td>17P; cerclage (if cervix &lt; 25 mm, 16-23 wks)</td>
</tr>
<tr>
<td>Singleton</td>
<td>Multiple</td>
<td>unclear; consider 17P</td>
</tr>
<tr>
<td>Singleton</td>
<td>No</td>
<td>not 17P candidate</td>
</tr>
<tr>
<td></td>
<td></td>
<td>vaginal progesterone if cervix &lt; 25 mm</td>
</tr>
<tr>
<td>Multiple</td>
<td>Singleton</td>
<td>unclear; consider 17P</td>
</tr>
<tr>
<td>Multiple</td>
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<td>unclear</td>
</tr>
<tr>
<td>Multiple</td>
<td>No</td>
<td>not 17P candidate</td>
</tr>
<tr>
<td>Multiple</td>
<td>----------</td>
<td>cervix &lt; 25 mm: NO cerclage</td>
</tr>
<tr>
<td></td>
<td></td>
<td>consider vaginal progesterone</td>
</tr>
</tbody>
</table>

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References

- Meis et al. NEJM 2003;348:2379-85
References

- **ACOG:**

- [www.marchofdimes.org](http://www.marchofdimes.org)
Questions?

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