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

UNC Center for Maternal & Infant Health

Community Care of North Carolina

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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Learning Objectives

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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

* 2007 IOM (www.marchofdimes.org/mission/the-economic-and-societal-costs.aspx)

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2014 March of Dimes Report Card

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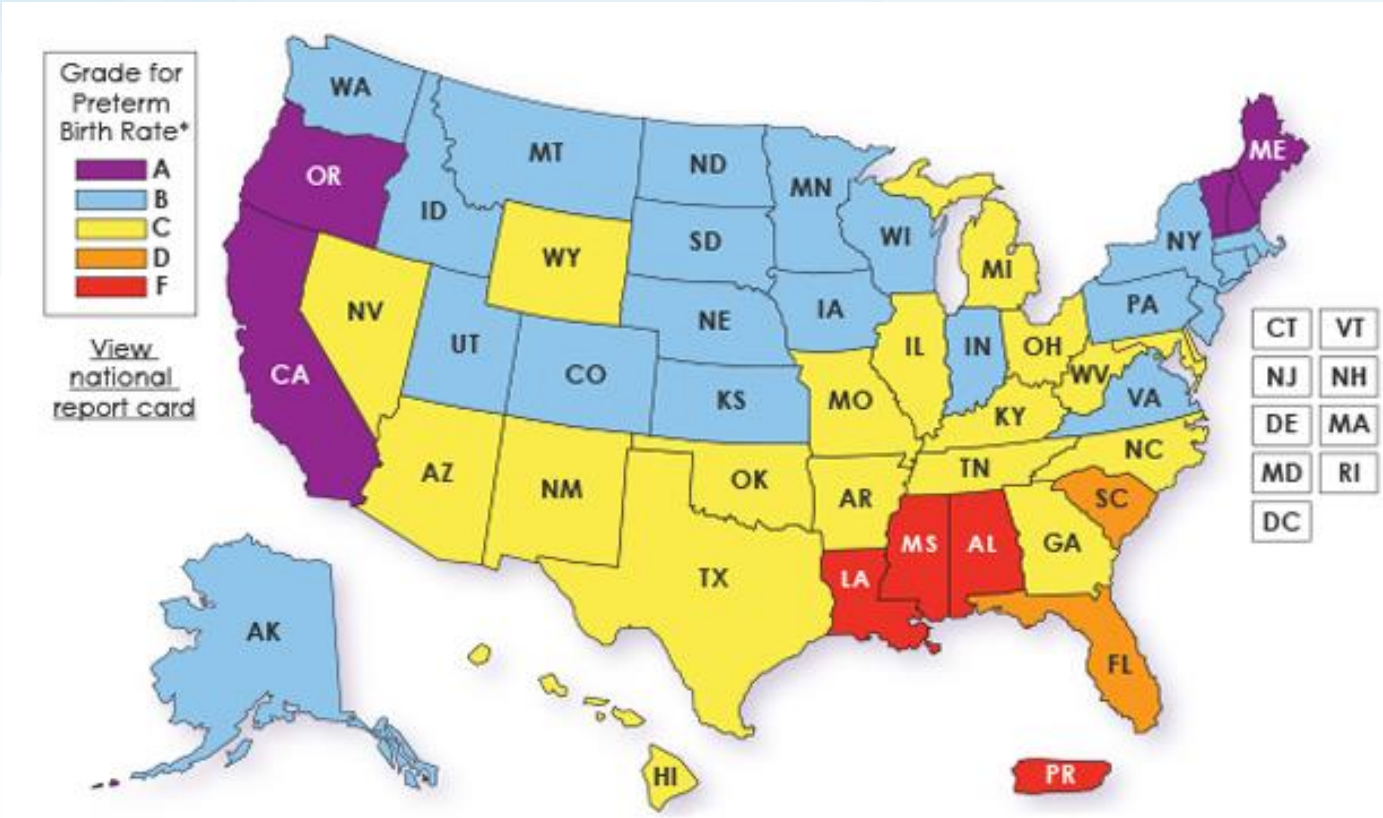
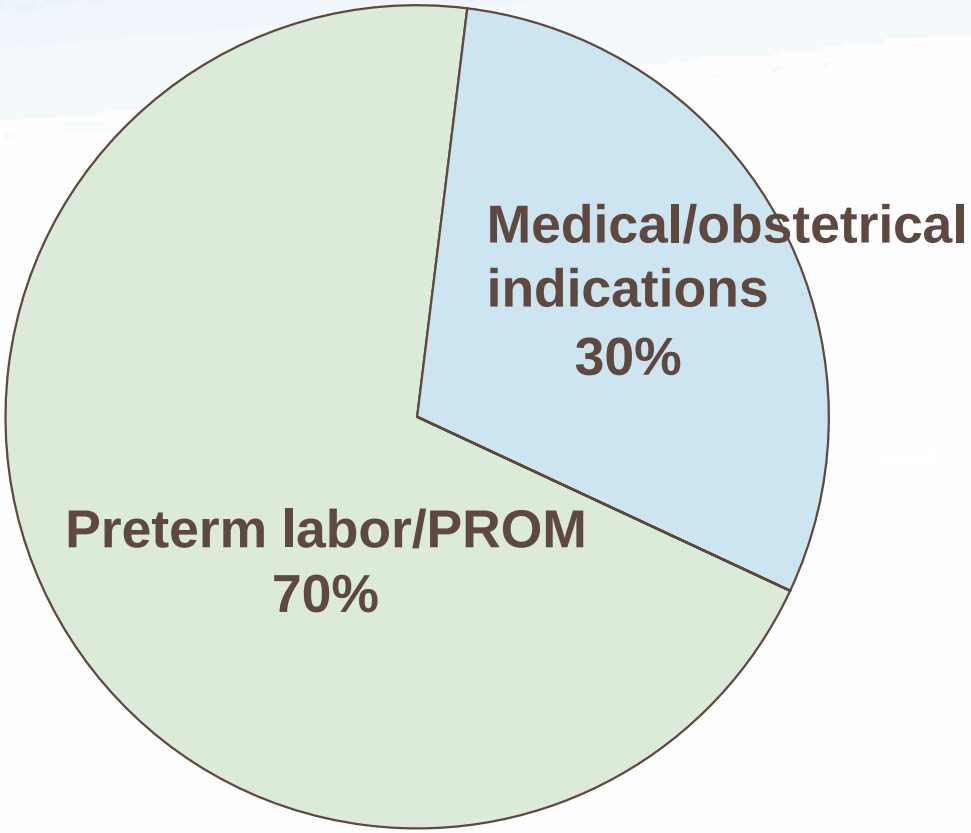


North Carolina	2006	2010	2014	2020 Goal
Preterm (< 37 weeks)	13.6%	12.7%	12.0%	9.6%

Preterm Birth: Etiology



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Recurrence Risks for Spontaneous Preterm Birth

	Risk of SPTB in next pregnancy
2nd pregnancy; 1st at term	9%
2nd pregnancy; 1st SPTB	22%
3rd pregnancy; 2 Prior SPTBs	42%
both < 32 weeks	57%
3rd pregnancy; 2 Term births	5%

Mercer (1999)

McManemy (2007)

Progesterone Therapy

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Two different preparations *with* two different indications

17P:

- prior spontaneous preterm birth

Vaginal progesterone:

- incidentally detected short cervix (ultrasound)

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17α-hydroxyprogesterone (17P)

Evidence supporting 17P

- **NICHD randomized controlled trial (2003)**

Eligible participants:

- **Prior spontaneous preterm birth 20^0 – 36^6**
- **Enrolled at 16-20 weeks**
- **Weekly 17P (250 mg) vs. placebo until 36 weeks**

Meis (2003)

Evidence for 17P

Gestation value	Placebo	17P	RR	P value
< 37 weeks	55%	36%	0.66	0.001
< 35 weeks	31%	21%	0.67	0.017
< 32 weeks	20%	11%	0.58	0.018

Approximately 33% reduction in preterm births

Meis (2003)

ACOG Practice Bulletin 130 (2012)

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Initial recommendation (2008)

Progesterone (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

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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

Vaginal Progesterone

Evidence for Vaginal Progesterone

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- **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

Progesterone:	**19%**	**(44% reduction)**
Placebo:	**34%**	

Fonseca (2007)

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ACOG Committee Opinion 522 (2012)

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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

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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)

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)

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Summary

Recommendations: Singleton gestation

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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

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Recommendations: Singleton gestation

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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

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Recommendations:
Multiple gestation

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Prior SPTB:

- consider 17P

Short cervix:

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

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Grand Summary

Current pregnancy	Past SPTB	Recommendation
Singleton	Singleton	17P; cerclage (if cervix < 25 mm, 16-23 wks)
Singleton	Multiple	unclear; consider 17P
Singleton	No	not 17P candidate vaginal progesterone if cervix < 25 mm
Multiple	Singleton	unclear; consider 17P
Multiple	Multiple	unclear
Multiple	No	not 17P candidate
Multiple	-------	cervix < 25 mm: NO cerclage consider vaginal progesterone

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References

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- Fonseca et al. NEJM 2007;357:642-9.
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  - Prediction and prevention of preterm birth. Practice Bulletin No. 130. October 2012
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  - Cerclage for the management of cervical insufficiency. Practice Bulletin No. 142. February 2014

- www.marchofdimes.org

Questions?

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