



Diagnosis and Management of Preterm Labor and Birth

SHANNON LEIGH SON, MD
FELLOW, MATERNAL-FETAL MEDICINE
UNIVERSITY OF UTAH HEALTH

Disclosure

- ▶ I have no conflicts to disclose

Objectives

At the end of this lectures, listeners can expect to be able to:

- ▶ Determine which patients are at increased risk of preterm birth
- ▶ Develop an effective strategy in evaluating patients with concern for preterm labor
- ▶ Manage patients with preterm labor
- ▶ Understand how preterm birth may be recurrent
- ▶ Conceptually understand management recommendations for future pregnancies

Why do we care?

- ▶ 9.63% of neonates are born preterm
 - ▶ 2.76% born at <34 weeks
 - ▶ 50% of these births were preceded by preterm labor
- ▶ Preterm labor is the leading cause for antenatal admission
- ▶ Incredible health care cost antepartum, intrapartum, and postnatally.

Why do we care?

- ▶ Preterm birth is the leading cause of neonatal mortality
 - ▶ 70% of neonatal deaths
 - ▶ 36% of infant deaths
 - ▶ 25-50% of long term neurologic impairment

Definitions

- ▶ Preterm labor (PTL)
 - ▶ Gestational age (GA) <37 weeks
 - ▶ Regular uterine contractions with change in cervical exam (dilation or effacement). -OR-
 - ▶ Regular contractions and an exam of at least 2cm dilation on presentation
- ▶ Preterm birth (PTB)
 - ▶ Delivery <37 weeks GA

Pathogenesis

- ▶ Stress (medical, social, maternal/fetal) → early hormonal activation
- ▶ Infection/inflammation-may account for 25-40%
 - ▶ Not just intrauterine infections!
 - ▶ The earlier the birth, the more likely it was related to infection
- ▶ Abruptio (decidual hemorrhage)
- ▶ Uterine anomalies or distension
- ▶ Cervical insufficiency
- ▶ Genetics

Historical risk factors

- ▶ Demographics
 - ▶ Race and Ethnicity, socioeconomic status, education, extremes of age, single marital status
- ▶ Obstetric history
 - ▶ **History of preterm birth** (and what happened since then?)
 - ▶ Recurrence risk: 15-50% depending on etiology and number of affected pregnancies
 - ▶ Short inter-pregnancy interval

Historical risk factors

- ▶ Maternal medical conditions
 - ▶ Low pre-pregnancy BMI, nutrient deficiencies, thyroid disease, asthma, hypertension, diabetes
 - ▶ Anxiety or stress, substance/tobacco use
- ▶ Pregnancy characteristics
 - ▶ Multifetal gestation
 - ▶ Placental issues
 - ▶ Uterine/cervix issues

Who is going to actually have a preterm birth?

- ▶ This is tough!
- ▶ <10% of women with a diagnosis of PTL deliver within 7 days.
- ▶ Let's collect some more information

Start with a thorough history

- ▶ Medical history
- ▶ OB history
- ▶ GYN history
- ▶ Current pregnancy complications
- ▶ Current symptoms

Physical Exam

- ▶ Vital signs
- ▶ Sterile speculum exam
 - ▶ Components both visual and specimen collection
- ▶ Cervical exam
 - ▶ It isn't just about the dilation
- ▶ Palpation of contractions, evaluate for tenderness
- ▶ Fetal heart rate tracing and tocometer

Ultrasound Utility

- ▶ Abdominal Ultrasound
 - ▶ Unknown or unclear GA
 - ▶ Unknown placental location
 - ▶ Fetal position
 - ▶ Evaluation of fluid
- ▶ Transvaginal ultrasound
 - ▶ Cervical length-utility diminishes with higher GA

Fetal fibronectin

- ▶ Fetal fibronectin-mixed opinions
 - ▶ Not useful as an isolated test
 - ▶ Most useful when only used with a cervical length 2-3cm
 - ▶ False positives possible if semen in vagina, recent SVE, or blood in vagina

Lab tests-depend on the differential diagnosis

- ▶ Urinalysis
- ▶ Wet prep
- ▶ Gonorrhea/chlamydia
- ▶ CBC
- ▶ +/-fFN

Management of PTL

- ▶ It depends on the gestational age!
- ▶ If viable (24 0/7*)
 - ▶ Monitoring
 - ▶ Admission for observation
 - ▶ Intervention
 - ▶ Corticosteroid administration (Betamethasone) (<36 6/7)
 - ▶ Magnesium sulfate (<32 0/7 GA)
 - ▶ Tocolysis (<34 0/7)
- ▶ Consultation
 - ▶ Maternal-Fetal Medicine depending on the context
 - ▶ Neonatalology

Corticosteroid administration

- ▶ This is the #1 thing to improve neonatal outcomes in PTB
 - ▶ Respiratory distress syndrome RR 0.66; 95% CI 0.59-0.73
 - ▶ Intracranial hemorrhage RR 0.54; 95% CI 0.43-0.69
 - ▶ Necrotizing enterocolitis RR 0.46; 95% CI 0.29-0.74
 - ▶ Death RR 0.69; 95% CI 0.58-0.81

Corticosteroid administration

- ▶ Medication: Betamethasone 12mg IM q24 hours for 2 doses
- ▶ Standard criteria:
 - ▶ 23 0/7-34 0/7 with anticipated delivery within 7 days
- ▶ Updated recommendation based on ALPS trial:
 - ▶ 34 0/7-36 6/7 with anticipated delivery within 7 days and have NOT already received a steroid course

Corticosteroid administration

- ▶ Consider a rescue dose if:
 - ▶ ≥ 2 weeks since the last dose (some consider 1 week)
 - ▶ < 34 weeks GA
 - ▶ At risk of delivery within the next 7 days
- ▶ Cochrane review in 2015 evaluated 10 trials, 5700 neonates
 - ▶ Additional dose(s) of corticosteroids resulted in:
 - ▶ \downarrow Respiratory distress syndrome (RR 0.83 95%CI 0.75-0.91)

Magnesium Sulfate

- ▶ Exposure to magnesium sulfate has been shown to:
 - ▶ ↓ Risk of cerebral palsy (RR 0.71, 95% CI 0.55-0.91)
- ▶ Recommended for women with preterm labor at <32 weeks
- ▶ Contraindications:
 - ▶ Myasthenia gravis
 - ▶ Pulmonary edema

Magnesium Sulfate

- ▶ Dosing:
 - ▶ Typically a bolus followed by maintenance
 - ▶ Bolus: 4-6g IV
 - ▶ Maintenance: 2g/hr IV
 - ▶ How long? When to stop? When to restart?
 - ▶ This is NOT well defined
 - ▶ Some hospitals give for 12 hours, others continue for 24 hours
 - ▶ Some hospitals restart at every hint at labor, others wait until delivery is imminent

Tocolysis

- ▶ May help to prolong pregnancy approximately 48 hours
 - ▶ Consider short term (48h) use if 24w-34w GA
- ▶ May help you get the patient transported, if needed, to a higher level of care

Tocolysis

- ▶ Contraindications (conditions that make prolonging pregnancy dangerous):
 - ▶ Fetal:
 - ▶ Demise, lethal anomalies, non-reassuring status
 - ▶ Maternal:
 - ▶ Pre-eclampsia with severe features, eclampsia, heavy vaginal bleeding with hemodynamic instability
 - ▶ Medication specific contraindications (see next slide)
 - ▶ Combined conditions:
 - ▶ Chorioamnionitis
 - ▶ PPROM*

Tocolytic agents

Table 1. Common Tocolytic Agents ↵

Agent or Class	Maternal Side Effects	Fetal or Newborn Adverse Effects	Contraindications
Calcium channel blockers	Dizziness, flushing, and hypotension; suppression of heart rate, contractility, and left ventricular systolic pressure when used with magnesium sulfate; and elevation of hepatic transaminases	No known adverse effects	Hypotension and preload-dependent cardiac lesions, such as aortic insufficiency
Nonsteroidal anti-inflammatory drugs	Nausea, esophageal reflux, gastritis, and emesis; platelet dysfunction is rarely of clinical significance in patients without underlying bleeding disorder	In utero constriction of ductus arteriosus*, oligohydramnios*, necrotizing enterocolitis in preterm newborns, and patent ductus arteriosus in newborn†	Platelet dysfunction or bleeding disorder, hepatic dysfunction, gastrointestinal ulcerative disease, renal dysfunction, and asthma (in women with hypersensitivity to aspirin)
Beta-adrenergic receptor agonists	Tachycardia, hypotension, tremor, palpitations, shortness of breath, chest discomfort, pulmonary edema, hypokalemia, and hyperglycemia	Fetal tachycardia	Tachycardia-sensitive maternal cardiac disease and poorly controlled diabetes mellitus
Magnesium sulfate	Causes flushing, diaphoresis, nausea, and reflexes, arrest, sup- contractility and left systolic	Neonatal depression‡	Myasthenia gravis
	causes profound neuromuscular blockade when used with calcium-channel blockers		

Rarely used

Not used as a tocolytic!

Other potential treatments

- ▶ Bed rest
 - ▶ Has not been demonstrated to help and has been demonstrated to have maternal harm
- ▶ Adequate hydration-Probably doesn't work but low harm

When do you discharge them?

(Assuming no further cervical change during the admission)

- ▶ After completion of betamethasone window (48 hours)?
- ▶ When they stop feeling contractions?
- ▶ When they achieve a particular gestational age?
- ▶ When they decide to move next door to the hospital?
- ▶ Never?

When do you discharge them?

- ▶ It is complicated!
- ▶ Through the betamethasone window is a good starting point
- ▶ Consider patient specific factors:
 - ▶ Gestational age
 - ▶ History
 - ▶ Concomitant medical conditions
 - ▶ Patient reliability
 - ▶ Proximity to the hospital
 - ▶ Closest hospital available to them-how early can they deliver?

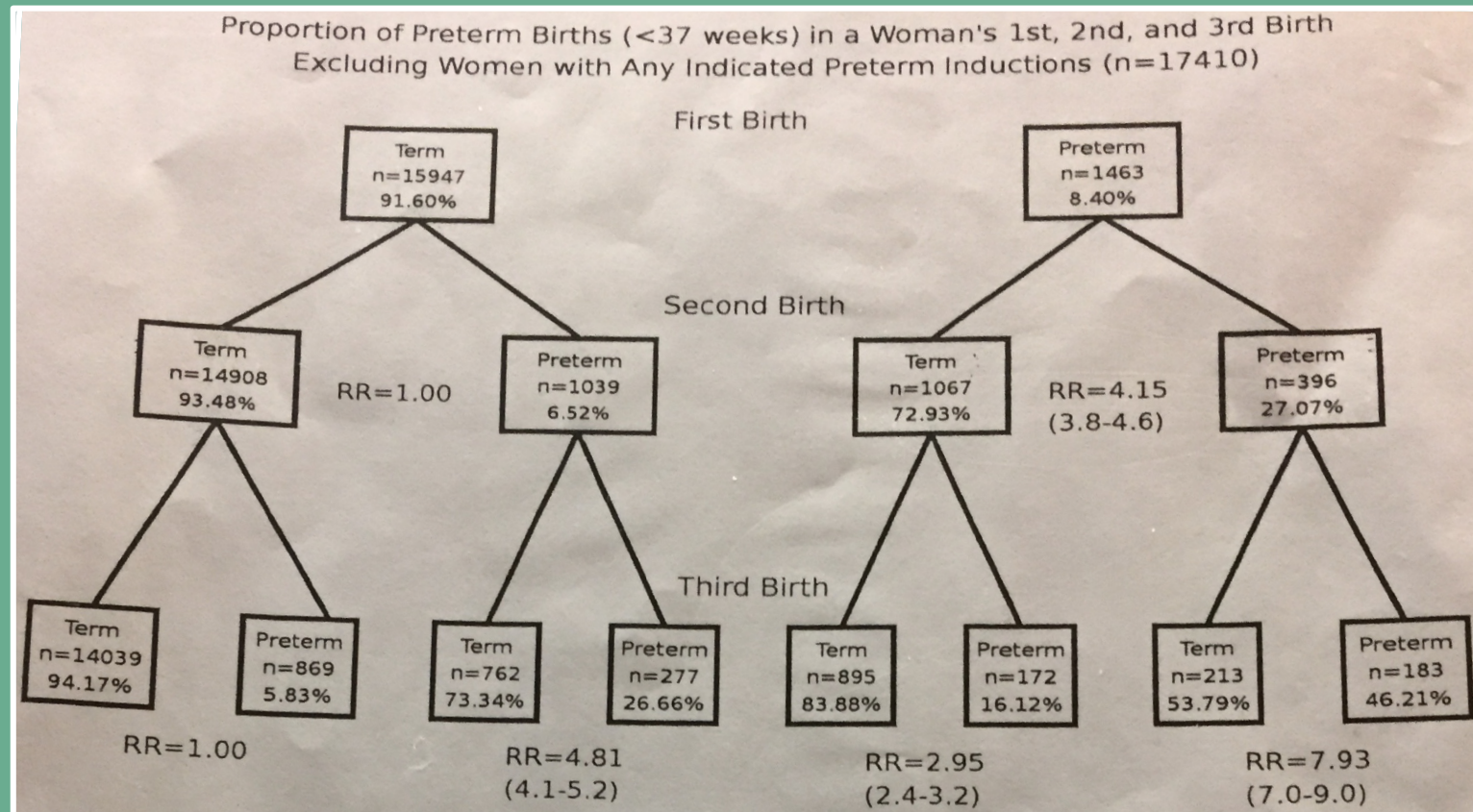
What about next time?

- ▶ Ideally in a pre-conception (typically Maternal-Fetal Medicine) counseling visit discuss:
 - ▶ Patient experience with preterm birth
 - ▶ Pregnancy spacing-18-23months
 - ▶ Healthy habits
- ▶ What is the recurrence risk?
 - ▶ Remember, it depends on the etiology
 - ▶ Preterm labor after a trauma does not carry the same recurrence risk as a patient with an unprovoked preterm birth

She's pregnant again-what now?

- ▶ Consultation with Maternal-Fetal Medicine early in pregnancy
 - ▶ Evaluation of appropriateness for serial cervical lengths, progesterone injections, cerclage
- ▶ Thresholds are institution dependent, particularly above 36 weeks GA
- ▶ Serial cervical lengths-Every 2 weeks from 16-24 weeks
 - ▶ Goal: early diagnosis of a shortening cervix that may benefit from cerclage
- ▶ 17-alpha-hydroxyprogesterone caproate-IM weekly from 16-36 weeks
- ▶ Healthy habits-weight, smoking

Recurrence Risk Estimates



What if the cervix shortens?

- ▶ If CL <25mm and patient is <24 weeks GA with a history of PTB, consider cerclage
- ▶ Cerclage in this population resulted in:
 - ▶ ↓ Deliveries < 24 weeks GA (RR 0.44; 95% CI 0.21-0.92)
 - ▶ ↓ Delivery <37 weeks (RR 0.75; 95% CI 0.60-0.93)
 - ▶ ↓ Perinatal death (RR 0.54; 95% CI 0.29-0.99)
 - ▶ ↓ Composite morbidity and mortality by 36% (16% vs 25%, RR 0.64; 95% CI 0.45-0.91)

Incidental short cervix without a history of preterm birth

- ▶ If CL \leq 20mm and \leq 24 weeks GA
 - ▶ Vaginal progesterone was associated with a 44% decrease in PTB $<$ 34w
 - ▶ Dosing: 200mcg vaginally daily
 - ▶ Some data to suggest pessary placement may \downarrow PTB in this context
 - ▶ A larger study is ongoing to validate

ACOG Short Cervix Algorithm

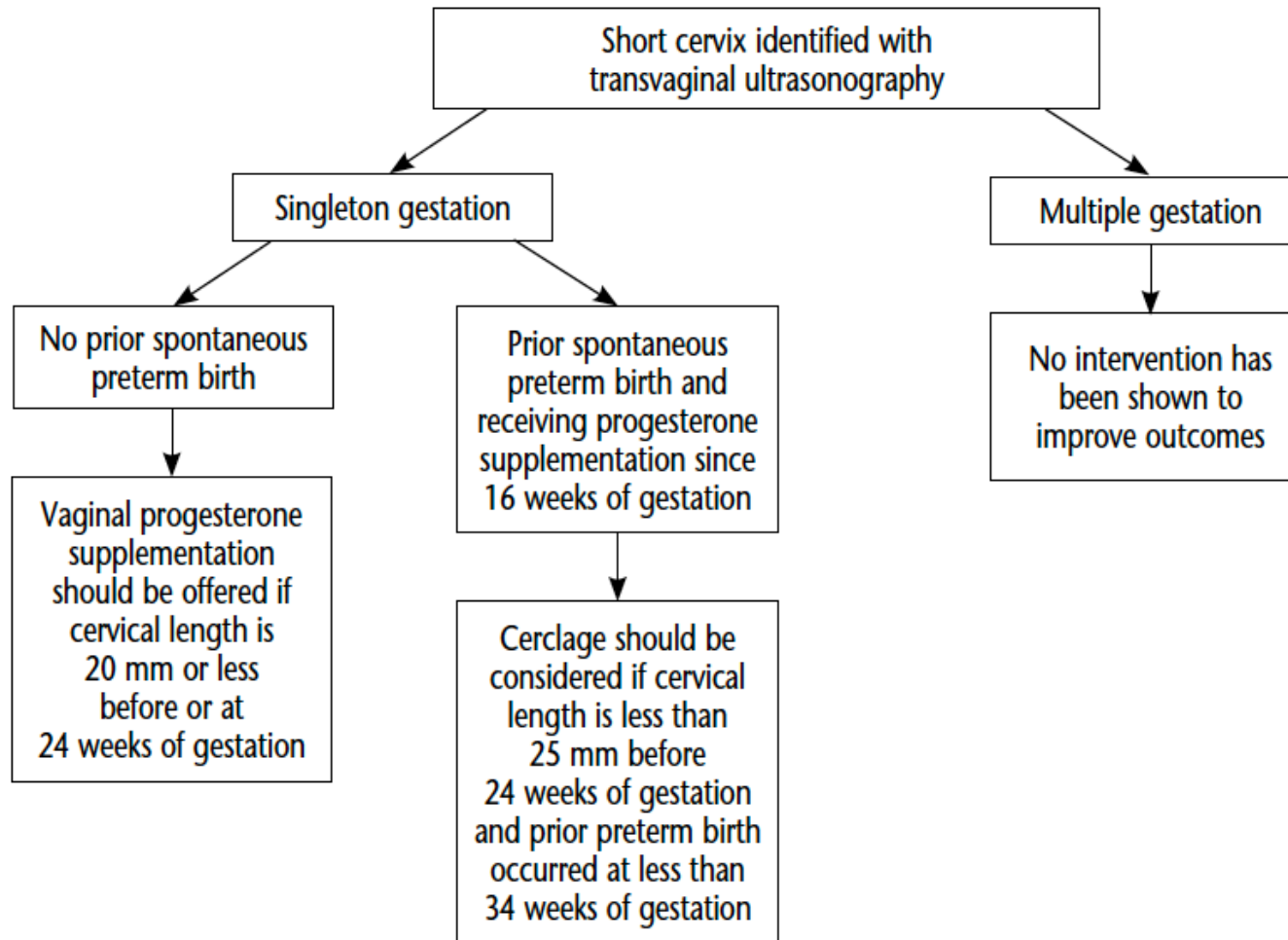


Fig. 1. Algorithm for the management of short cervical length in the second trimester. ↩

Twins? Triplets?

- ▶ Very limited data
- ▶ Cerclage for short cervix may increase PTB
 - ▶ RR 2.2; 95% CI 1.2-4

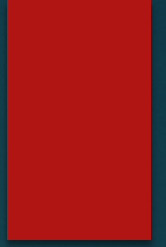
Case 1

- ▶ 25 yo G2P0101 at 28 0/7 who presents to OBES for evaluation of intermittent contractions and spotting.
- ▶ What else do you want to know?
- ▶ What exam would you perform?
- ▶ What tests would you perform?
- ▶ What interventions would you offer?

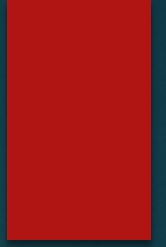
Case 2

- ▶ 28yo G4P2103 at 33 3/7 who presents with spotting and on exam has a cervical exam of 2/thick/high, posterior but soft.
- ▶ What else do you want to know?
- ▶ What additional exam would you perform?
- ▶ What tests would you perform?
- ▶ What interventions would you offer?

Additional cases?



Questions?



References

- ▶ Martin JA, Hamilton BE, Osterman MJ, Driscoll AK, Mathews TJ. Births: final data for 2015: Natl Vital Stat Rep 2017;66(1):1-70.
- ▶ Goldenberg RL, Culhane JF, Iams JD, Romero R. Epidemiology and causes of preterm birth. Lancet 2008. 371:75-84.
- ▶ Prediction and Prevention of Preterm Birth. ACOG Practice Bulletin No. 130. American College of Obstetricians and Gynecologists. Obstet Gynecol 2012, reaffirmed 2018;120:964-973.
- ▶ Management of Preterm Labor. ACOG Practice Bulletin No. 171. American College of Obstetricians and Gynecologists. Obstet Gynecol 2016, reaffirmed 2018;128:e155-964
- ▶ Sheiner E, Mazor-Drey E, Levy A. Asymptomatic bacteruria during pregnancy. J Matern Fetal Neonatal Med 2009; 22:423.
- ▶ Smaill F. Antibiotics for asymptomatic bacteruria in pregnancy. Cochrane Database Syst Rev 2001: CD000490
- ▶ Nygren P, Fu R, Freeman M, et al. Evidence on the benefits and harms of screening and treating pregnant women who are asymptomatic for bacterial vaginosis: an update review for the U.S. Preventative Services Task Force. Ann Intern Med 2008; 148:220.
- ▶ Fuchs IB, Henrich W, Osthues K, Dudenhausen JW. Sonographic cervical length in singleton pregnancy with intact membranes presenting with threatened preterm labor. Ultrasound Obstet Gynecol 2004;24:554-7.
- ▶ Roberts D, Dalziel SR. Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth. Cochrane Database of Systematic Reviews 2006. Issue 3. Art, No, CD004454. DOI: 10.1002/14651858.
- ▶ Crowther CA, McKinlay CJ, Middleton P, Harding JE. Repeat doses of prenatal corticosteroids for women at risk of preterm birth for improving neonatal health outcomes. Cochrane Database of Systematic Reviews 2015. Issue 7. Art. No.: CD003935. DOI: 10.1002/14651858.CD003935.pub4.
- ▶ Conde-Agudelo A, Romero R. Antenatal magnesium sulfate for the prevention of cerebral palsy in preterm infants less than 34 weeks gestation: a systematic review and metaanalysis. Am J Obstet Gynecol 2009;200:595-609.
- ▶ Owen J, Hankins G, Iams JD, Berghella V, Sheffield JS, Perez-Delboy A, et al. Multicenter randomized trial of cerclage for preterm birth prevention in high-risk women with shortened midtrimester cervical length. Am J Obstet Gynecol. 2009;201:375.e1-8
- ▶ Fonseca EB, Celik E, Parra M, Singh M, Nicolaides KH. Progesterone and the risk of preterm birth among women with a short cervix. Fetal Medicine Foundation Second Trimester Screening Group. N Engl J Med 2007;357:462-469.
- ▶ Berghella V, Odibo AO, To MS, Rust OA, Althuisius SM. Cerclage for short cervix on ultrasonography: meta-analysis of trials using individual patient-level data. Obstet Gynecol 2005;106:181-189.

Thank you!

