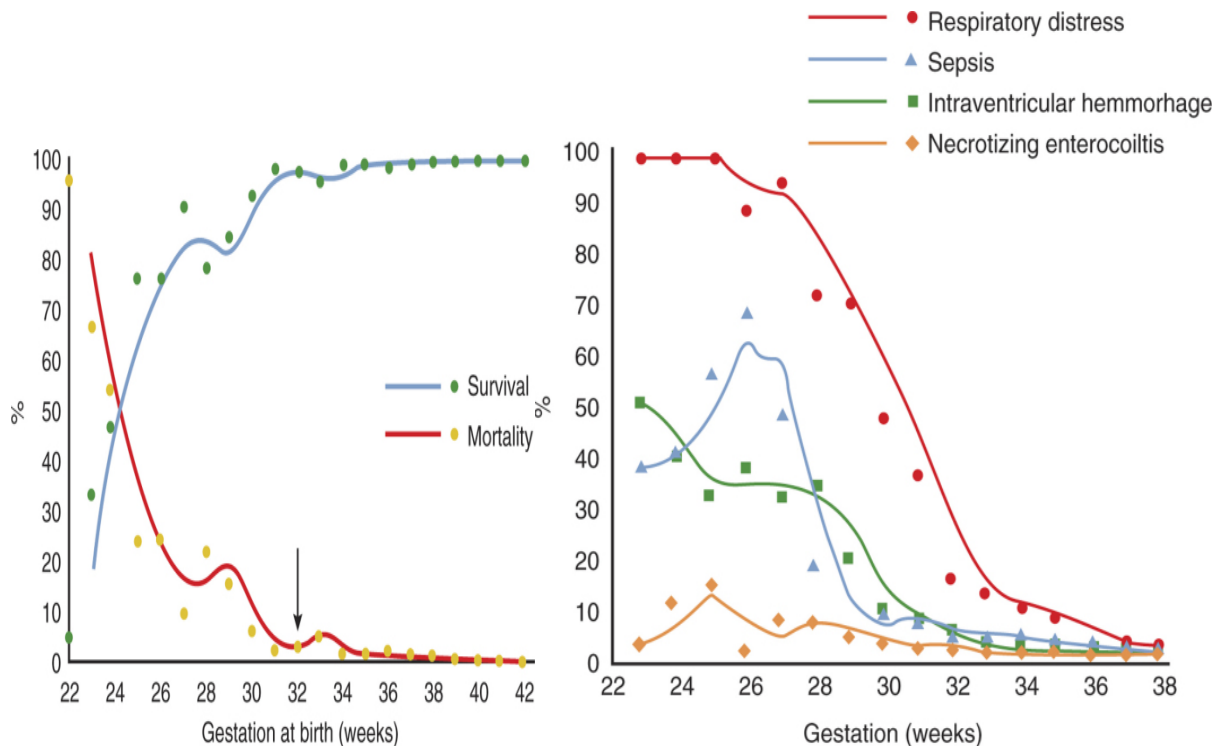


## Preterm Labor & Delivery

### RATIONALE

The rate of preterm birth in the United States has been rising over the last 15 years. Nationally, preterm birth affects 12% of all babies delivered in the United States or approximately 480,000 births. In the last decade, preterm birth has increased by 27% in the United States and accounts for 85% of all perinatal morbidity and mortality. Preterm birth is the leading cause of perinatal mortality among African Americans and the second leading cause among the overall American population. 75% of all preterm deliveries are spontaneous and the other 25% are iatrogenic for obstetric indications or elective in nature. Although there is no test to accurately predict who will delivery preterm, women at greatest risk for preterm birth have a history of preterm delivery.



(L) Figure 26-3 Perinatal mortality and gestational age. (Modified from Mercer BMM: Preterm premature rupture of the membranes. *Obstet Gynecol* 101:178, 2003.)

(R) Figure 26-5 Survival and mortality rates for 8,523 infants born in 1997 to 1998 at a single U.S. center. (From Mercer BMM: Preterm premature rupture of the membranes. *Obstet Gynecol* 101:178, 2003.)

## **DEFINITIONS**

**Term:** between 38 to 42 completed weeks of gestation

**Preterm:** before the completion of 37 menstrual weeks of gestation

**Premature Rupture of Membranes (PROM):** rupture prior to the onset of labor

**Preterm Premature Rupture of Membranes:** PROM prior to 37 wks gestation

## **PREVENTION OF PRETERM BIRTH**

### ***Public Health Model***

**PRIMARY:** prevention and reduction of risk in the population

- ❖ No test with ideal sensitivity or predictive value
- ❖ Treat STD & Stop Smoking

**SECONDARY:** identification and treatment for individuals with increased risk

- ❖ History of preterm birth
- ❖ 17- $\alpha$  hydroxyprogesterone caproate IM weekly

**TERTIARY:** treatment initiated after the labor process has begun to limit perinatal morbidity and mortality

- ❖ Acute tocolysis + corticosteroids + NICU
- ❖ Treat Group B Strep
- ❖ MgSO<sub>4</sub> for fetal neuroprotection

### **Risk Factors for Spontaneous PTD (75%)**

- ❖ Hx of preterm delivery
- ❖ Preterm ruptured membranes
- ❖ Nonwhite race
- ❖ Multiple gestation
- ❖ Bleeding after the 1st trimester
- ❖ Low prepregnancy weight (<110 lbs)
- ❖ Infections (genital and systemic)
- ❖ Elective (non-medical indicated) deliveries < 39
- ❖ Smoking
- ❖ > 50% with PTD have NO risk factors

### **Diagnosing PTL**

Accurate early diagnosis of preterm labor is *elusive*

- ❖ 50% diagnosed with PTL do not actually deliver prematurely
- ❖ 20% symptomatic patients diagnosed as not having PTL deliver prematurely.
- ❖ Early signs and symptoms are imprecise and become clear only when in full blown active PTL (pains & gains are observed)
- ❖ Optimal criteria for initiation of “treatment” are not clear

### **Early Detection of PTL**

Theory- early diagnosis of preterm labor and intervention with tocolytic drugs would be more effective if given before significant cervical change occurs. Large randomized controlled trials in women at risk using outpatient HUAM accompanied by daily nursing contact found no effect on the rate of preterm birth or neonatal outcomes. The largest such trial randomized more than 2,400

women and found no effect of close monitoring of symptoms or contractions on rates of preterm birth or eligibility for tocolysis.

### **Clinical Evaluation for Possible PTL**

1. **Patient presents with signs/symptoms of PTL:**

- Persistent contractions (painful or painless)
- Intermittent abdominal cramping, pelvic pressure, or backache
- Increase or change in vaginal discharge
- Vaginal spotting or bleeding

2. **General physical examination:**

- Pulse and blood pressure, temperature, external fetal heart rate and contraction monitoring

3. **Sterile speculum examination**

pH, Ferning pattern, Pooled fluid, Fibronectin swab (posterior fornix or external cervical os, avoiding areas with bleeding), Testing for chlamydia & GC, and group B streptococcus

4. **Transabdominal ultrasound examination**

Placental location  
Amniotic fluid volume  
Estimated fetal weight and presentation  
Fetal well being

5. **Cervical examination** (after ruptured membranes excluded)

**a. Cervix  $\geq 3$  cm dilation /80% effaced**

PTL diagnosis confirmed  $\diamond$  Evaluate for tocolysis

**b. Cervix 2 to 3 cm dilation / < 80% effaced**

PTL likely but **not** established. Monitor contraction frequency & repeat digital examination in 30–60 minutes. Diagnose PTL if cervical change. If not, send fFN &/or obtain transvaginal cervical ultrasound (TVU). Evaluate for tocolysis if any cervical change, cervical length <2cm or +fFN

**c. Cervix <2 cm dilation and <80% effaced**

PTL diagnosis uncertain. Monitor contraction frequency, send fFN &/or obtain TVU, and repeat digital examination in 1 to 2 hours. Evaluate for tocolysis if there is a 1cm change in cervical dilation, effacement >80%, cervical length <2 cm or + fFN

6. **Use of Cervical Ultrasound**

Cervical length <20 mm *and* contractions => **PTL**

Cervical length 20–30 mm *and* contractions => **probable PTL**

Cervical length >30 mm => **PTL very unlikely, regardless of contraction frequency**

### **GOALS OF TREATMENT FOR WOMEN IN PRETERM LABOR**

**ONLY 3 interventions have been proven to reduce perinatal morbidity and mortality:**

1. **Transfer** of the mother and fetus to an appropriate hospital with a NICU
2. Administration of **antibiotics to prevent neonatal GBS infection** (ampicillin or erythromycin)
3. Administration of **corticosteroids** to reduce neonatal RDS and intraventricular hemorrhage

- “Acute” tocolysis is indicated to delayed delivery for 48 hours to allow antenatal transport and corticosteroids to reduce neonatal morbidity and mortality
- Meta-analyses of studies of individual tocolytic drugs typically report limited prolongation of pregnancy (2-7 days) but no decrease in PTD
- Limited data whether prolongation of pregnancy was accompanied by improved infant outcomes or true cost savings
- **No** evidence of benefit for maintenance tocolysis (oral or pump)

### **Treatments**

- ◆ **Antimicrobial therapy** of women in preterm labor should be limited to GBS prophylaxis, women with preterm PROM, or treatment of a specific pathogen
- ◆ **Antenatal Corticosteroids** betamethasone and dexamethasone are the only drugs found beneficial. Treatment: 2 doses of betamethasone 12 mg IM 24 hours apart, or four doses of dexamethasone 6 mg IM every 12 hrs 2 doses
- ◆ **Tocolytics-**
  - Calcium channel blockers and oxytocin antagonists can delay delivery by 2 to 7 days with the most favorable benefit/risk
  - Terbutaline can delay delivery by 48hrs but has > side effects
    - Terbutaline was once the most commonly used tocolytic but is being replaced by drugs with better safety and side effect profiles
    - Terbutaline relatively few serious side effects when used as a single subcutaneous injection of 0.25 mg to facilitate maternal transfer or to initiate tocolysis, while another agent with a slower onset of action is being given
  - Long-term oral (maintenance) or subcutaneous treatment has ***not*** been shown in controlled trials to reduce prematurity or neonatal morbidity
  - COX inhibitors (Indomethacin) effective, generally well tolerated, concern about fetal side effects limited use to brief therapy before 32 weeks
  - Magnesium sulfate is ineffective but may be a useful choice when the diagnosis of preterm labor is early and uncertain, and in patients in whom other agents are contraindicated, for example, in patients with insulin-dependent diabetes.
    - ❖ **Contraindications to tocolysis:**
      - Maternal hypertension (acute hypertensive crises), bleeding (placenta previa and abruption), and cardiac disease ( $\beta$ -Mimetic agents and calcium channel blockers interfere with maternal cardiovascular response to hypotension, and prostaglandin inhibitors are known to impair maternal platelet function.
      - Fetal contraindications include gestational age of greater than 37 weeks, fetal demise or lethal anomaly, chorioamnionitis, and evidence of acute or chronic fetal compromise.

### **Care After Acute Treatment for Preterm Labor**

- **Maintenance Tocolytic Treatment** after acute tocolysis does not reduce the rate of preterm birth, does not prolong pregnancy or decrease the frequency of preterm birth.
- **Post-hospitalization Surveillance** with outpatient monitoring of uterine contractions (HUAM) did not improve the rate of delivery before 37 weeks, birth weight, or gestational age at delivery in any of three randomized trials or in a meta-analysis.

- ❖ A multicenter randomized trial in which uterine activity was monitored but the data were ignored in one group found no improvement in preterm birth rate when contraction data were used.
- ❖ Benefit observed with high patient touch by nurses (TLC)

**Clinical Predictors of PTD**

50 % PTD have **NO** apparent clinical risk factors!

- multiple gestation (RR 5-6 fold)
- history of preterm birth (RR 2-4 fold)
- vaginal bleeding after the first trimester (RR 3 fold)
- low pre-pregnancy weight, GU track colonization or infection, and black ethnicity (RR 1.5-2 fold)

**Mode of Delivery**

Routine cesarean delivery of all preterm or VLBW infants is not justified nor is the use of forceps

**Studied Interventions to Prevent Preterm Birth in Asymptomatic Women**

- Vitamins
- Calcium
- Social Support
- Bed Rest
- Risk Scoring
- Maintenance Tocolysis
- Uterine Contraction Monitoring
- Cervical cerclage
- Antibiotics
- ❖ ***Progesterone- the only one with data to support it use***
  - ◆ 2 randomized trials that enrolled women with a previous preterm birth revealed a reduction in recurrent preterm by one third. When these studies were included in meta-analyses with earlier trials of supplemental progesterone, the risk of recurrent preterm birth was reduced by 40 to 55%

**Summary of Studies of Interventions to Prevent Preterm Birth in Asymptomatic Women**

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RISK FACTOR	INTERVENTION	STUDY	OUTCOME	REFERENCE
<b>Nutritional Deficiencies</b>				
<i>Calcium</i>	Calcium	RCT in 190	↓ PTB	Villar & Repke AJOG 1990
	Calcium	RCT in 456	↓ PTB	Crowther Aust NZ J Obstet Gynecol 1999
	Calcium	RCT in 4589	No Δ in PTB	Levine NEJM 1997
<i>Vitamins</i>	Vitamin C	RCT in 200	↑ in PTB	Steyn J Obstet Gynaecol

RISK FACTOR	INTERVENTION	STUDY	OUTCOME	REFERENCE
				2003
	Vitamin C	Meta-analysis of 766 in RCTs	No Δ in PTB, but ? ↑ in PTB	Rumbold & Crowther Cochrane Database 2006
	Vitamin E	Meta-analysis of 566 in RCTs	No Δ in PTB	Rumbold & Crowther Cochrane Database 2006
	Vitamins C + E	RCT in 2410 with risk of preeclampsia	No Δ in PTB ↑ in LBW	Poston et al Lancet 2006
	Vitamins C + E	RCT in 1877 in nulliparas	No Δ in PTB	Rumbold et al NEJM 2006
	Multivitamins	RCT peri-conception MV in 5502	No Δ in PTB	Czeizel Arch Gynecol Obstet 1994
<b>Social Support</b>				
	Nurse visits	RCT	↓PTB in teens <17 yrs old	Olds et al Pediatrics 1986
	Social support	RCT in 2235 women with increased risk	No Δ in PTB or LBW	Villar et al NEJM 1992
	Nurse visits	RCT in 1139 with social risk	No Δ in PTB or LBW	Kitzman et al JAMA 1997
	Teen prenatal clinics Social support	RCT in 651 teens	↓PTB	Quinlivan & Evans BJOG 2004
		Meta-analysis	No Δ in PTB or LBW	Hodnett & Fredericks Cochrane Database 2005
<b>Bed Rest</b>				
	Bed rest for women with twins or risk of PTB	Meta-analyses	No Δ in PTB or LBW	Goldenberg Obstet Gynecol Sosa Cochrane Database 2006
<b>Risk Scoring and Education</b>				
	Frequent visits and education for high risk women	RCT of 2395 women at 5 sites	No Δ in PTB or LBW	March of Dimes Collaborative AJOG 1993
<b>Maintenance Tocolysis</b>				
After treatment of preterm labor	Oral tocolysis subcutaneous pump	Meta-analyses of small RCT's	No Δ in PTB or LBW	Macones Obstet Gynecol 1995
				Sanchez-Ramos Clin Perinatol 2003
				Berkman AJOG 2003
				Dodd Cochrane Database

RISK FACTOR	INTERVENTION	STUDY	OUTCOME	REFERENCE
				2006
				Nanda Cochrane Database 2006
<b>Uterine Contraction Monitoring</b>				
	Monitoring contractions to detect recurrent preterm labor	3 RCT's in women treated for PTL	No Δ in PTB or LBW	Iams et al Am J Perinatol 1990
				Nagey et al Obstet Gynecol 1993
		Meta-analysis		Brown et al AJOG 1999
				Berkman et al AJOG 2003
	Monitoring contractions to detect early PTL	RCT in 2422 at risk of PTB	No Δ in PTB or LBW	Dyson et al NEJM 1998
				ACOG Practice Bulletin 31, Obstet Gynecol 2001
		Review		
<b>Cervical Cerclage</b>				
	Cervical cerclage	RCT in women with a prior PTB	Mixed but mostly negative results	MacNaughton BJOG 1993
				To et al Lancet 2004
		Reviews and meta-analyses		Owen et al AJOG 2003
				Drakeley et al Cochrane
			? benefit if no cervical inflammation*	Database 2006
				Berghella Obstet Gynecol 2005
		Observational study		Sakai et al AJOG 2006*
<b>Progesterone supplementation</b>				
	Progesterone	RCT in 142 women with risk	↓PTB	da Fonseca AJOG 2003
	17 α OH progesterone caproate	RCT in 459 women with a prior PTB	↓PTB	Meis et al NEJM 2003
		Meta-analyses	↓PTB	Dodd Acta Obstet Gynecol Scand 2005
				Sanchez Ramos Obstet Gynecol 2005

RISK FACTOR	INTERVENTION	STUDY	OUTCOME	REFERENCE
				Mackenzie AJOG 2006

LBW, low birth weight; PTB, preterm birth; RCT, randomized controlled trial.

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Management of preterm labor. ACOG Practice Bulletin No. 43. American College of Obstetricians and Gynecologists. Obstet Gynecol 2003; 101:1039-47. Reaffirmed 2008.