



[Color index: **Important** | [Notes](#) | Extra | [video case](#)]
Editing file [link](#)



Preterm labor

Objectives:

- Identify the modifiable and non-modifiable risk factors and causes for preterm labor.
- Describe the signs and symptoms of preterm labor.
- Describe the initial management of preterm labor.
- List indications and contraindications of medications used in preterm labor.
- List the adverse outcomes associated with preterm birth.
- Describe the counseling for reducing preterm birth risk.

References : 433 team, kaplan lecture notes 2018 + kaplan video note.

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Introduction

Definition:

Delivery between 20-37 wks of EGA that include **uterine contractions** + **cervical dilation** (at least 2 cm) or change in serial examination (in dilation or effacement).

DDx of **uterine contractions**:

- 1- preterm labor (if at least 3 in 30 min + cervical change or dilation)
- 2- uterine irritability (high frequency brief with no cervical changes)
- 3- Braxton & Hicks contractions
- 4- preterm contractions (same as preterm labor but no cervical changes or dilation)

Epidemiology:

Common, 12.7% of all deliveries in the United States.

The leading causes of morbidity and mortality in preterm labor are: **respiratory distress**, **Infection**, and **Intraventricular hemorrhage**.

Risk factors: the most important risk factors are previous history of preterm labour & cervical effacement

Prior history of preterm birth, 1.5-2x (highest risk)	African-American race (16.3%)
Short cervical length <25 mm (before 20 wks)	Preterm uterine contractions
Premature rupture of membranes (PROM)	Incompetent cervix (e.g. Hx of surgery)
Shortened cervix on transvaginal ultrasound	Infections (Urinary, Vaginal (BV), Intra-amniotic)
Maternal smoking (associated with PROM)	Substance abuse
Inflammation	Decidual hemorrhage
Pathologic uterine distension	Low pre-pregnancy BMI
Excessive uterine enlargement (Polyhydramnios, Multiple gestation)	
Uterine distortion (Leiomyomas, Septate uterus, uterine didelphis, and other anomalies)	
Placental abnormalities (Abruptio placentae, Placenta previa)	
Short interpregnancy intervals	
Vaginal bleeding, UTIs, genital tract infections, or Periodontal diseases.	

Diagnosis

Signs and symptoms:

- Lower abdominal pain or pressure
- lower back pain
- increased vaginal discharge, or bloody show.
- Particularly in primigravidas, the symptoms may be present for a number of hours to days but are not recognized as contractions by the patient.

Evaluations

1. **Vaginal examination** → cervical length, dilation, station, presentation.
2. **Swap/Culture for presence of Group B strep.**
3. CBC, Random Blood Glucose, Serum electrolytes levels ... etc.
4. Ultrasound → fetal weight, presentation, any congenital malformations, multifetal gestation, uterine anomalies.
5. Any underlying correctable conditions.
6. Put patient in lateral decubitus position.
7. Monitor uterine activity.

Diagnostics:

The diagnosis of preterm labor is by presence two things:

1. **True Uterine contractions** → 4/20 min. (Poor indicator of preterm labor)
2. **Cervical changes** → 80 % effacement or 2 cm dilation. (Good indicator)

Others: Vaginal swap fetal fibronectin (+ **Positive** in fetal membrane rupture, short cervix, infection).

Management¹:

- o **Short-term tocolytic therapy:** Used for prolongation of pregnancy (48h) for: **1-Corticosteroids to do its effect, 2-Mother transfer to better center in preterm baby care.**
- o **Tocolytic Contraindications.** These are conditions under which **stopping labor is either dangerous for mother and baby or futile** (makes no difference in outcome). Examples include the following:
 - **Obstetric conditions**—**severe abruptio placentae, ruptured membranes, chorioamnionitis.**
 - **Fetal conditions**—**lethal anomaly** (anencephaly, renal agenesis), **fetal demise or jeopardy** (repetitive late decelerations).
 - **Maternal conditions**—**eclampsia, severe preeclampsia, advanced cervical dilation.**
- o Nowadays, **Magnesium Sulfate** is widely used if delivery believed to be eminent < 32 weeks because of its effect in reducing the severity and risk of cerebral palsy and surviving infants. Others : Beta 2 agonist (terbutaline), CCB (Nifedipine) and Prostaglandin synthase inhibitor (indomethacin).

Sides effects :

TOCOLYTIC agents	
Agent	Side Effects
MgSO₄	Respiratory depression
β-Adrenergic Agonists	↑ Glucose ↓ Potassium
Ca⁺⁺ channel blockers	Myocardial depression
PG synthetase inhibitors	Oligohydramios IU closure PDA

- o If patient is 24-34 weeks EGA:
 - **Corticosteroids:** Most important to reduce the rates for Respiratory distress syndrome, Intracranial hemorrhage, Necrotizing enterocolitis, and death.

¹ In twin pregnancy no intervention shown to have any benefit (KAPLAN).

- **Progesterone** therapy can **reduce the risk of preterm labor: it causes inhibition of the cervical ripening, reduction of myometrium contractility it is used for prevention**, and it's a modulator of inflammation. It's usually given to women who have: 1. history of preterm labor, 2. Short cervix during pregnancy. (if cervical length < 1.5)

General tips:

1. **Hydration and bed rest** can resolve uterine contractions in 20% of patients.
2. **Antibiotic if there is infection or as prophylactic** (after take urine and cervical swab samples for cultures) ampicillin or erythromycin In case of penicillin allergy.
3. IV MgSO4 for fetal neuroprotection (also is Tocolytic).
4. If a patient doesn't respond to hydration and bed rest, give **Tocolytic** therapy.
5. **Betamethasone if <34w.**
6. **Delivery in Preterm labor is usually vaginally** (normally or using outlet forceps), except for very low-birth fetuses (<1500 g) where cesarean delivery is better, as in 28 wks. 23% of infants have breech presentation.
7. **Neonatal care unit that can help within viability limits** (24 wks. or greater than 500 g).

	Medications	MOA	Side effects	Contra-indications
Antibiotics	Ampicillin "penicillin-type"	Bacteriostatic,	Nausea, vomiting, diarrhea	
	Erythromycin "penicillin-type"	Bacteriostatic antibiotic macrolide, protein synthesis inhibitor.	Nausea, vomiting, diarrhea	
	Clindamycin "Use if allergy to penicillin"	Bacteriostatic, protein synthesis inhibitor.	Diarrhea	
Tocolytic agents	Magnesium Sulfate "Solution" less < 32 wks. of EGA	↓Ca ⁺⁺ by competing on cell entry. (myometrial relaxation)	Warmth, flushing at administration. Respiratory depression (level 12-15 mg/dL), cardiac conduction defects/arrest (higher levels). In neonates: low muscle tone, drowsiness and low APGAR score	Severe preeclampsia, Bleeding due to placenta Previa/abruption.
	Nifedipine "Oral"	Inhibit the slow inward Ca ⁺⁺ during 2 nd phase of Action potential.	Headache, flushing, hypotension, tachycardia.	IUGR,
	Indomethacin (Prostaglandin Synthetase Inhibitors)	Inhibits myometrial contractions. Short-term use only! Due to side effects	In neonates: Oligohydramnios, patent ductus arteriosus, necrotizing enterocolitis, intracranial hemorrhage.	fetal anomalies, Fetal demise.
	Atosiban (Oxytocin receptor antagonists)	Binds to receptors in myometrium, preventing inositol triphosphate that increases Ca ⁺⁺ levels.		
	Combined: Nifedipine + Prostaglandin Synthetase Inhibitors			
	Betamethasone, Dexamethasone (Glucocorticoids) 24-34 wks. of EGA	↑Fetus lung maturity, ↓ risk of RDS, intracranial hemorrhage, necrotizing enterocolitis		
	Progesterone supplements (injections, pills)	In case of Hx of preterm pregnancies.		

Note:

CCBs are contraindicated if Hypotensive or preload dependent cardiac lesions e.g. aortic insufficiency.

NSAIDs are contraindicated if platelets dysfunction, bleeding disorder, hepatic or renal dysfunction, GI ulcer, and asthma.

Magnesium sulfate is contraindicated in myasthenia gravis.

Beta-adrenergic receptor agonists are contraindicated if tachycardia-sensitive maternal cardiac disease and DM.

If indomethacin was used for >48h it causes closure of ductus arteriosus in utero.

Case



CASE:

An 18-year-old African-American, G2P0101 woman who is 12 weeks pregnant, presents to your prenatal clinic for a new patient visit. Before you walk into the room to see the patient, you look through her records and note that she delivered her last pregnancy just 12 months ago. Beginning at 24 weeks in her previous pregnancy, the patient presented numerous times to Labor and Delivery reporting contractions, and was sent home each time with a diagnosis of “Braxton-Hicks contractions.” She eventually presented at 28 weeks gestation and was diagnosed with preterm labor. She delivered at 29 weeks. The neonate’s course was complicated by intra-ventricular hemorrhage and respiratory distress syndrome. The child now appears to have cerebral palsy and chronic lung disease due to bronchopulmonary dysplasia

1. What are the risk factors for preterm labor, and which ones does this patient have?

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2. What characteristics distinguish Braxton-Hicks contractions from true labor contractions?

Braxton-Hicks contractions	True Labor Contractions
Irregular and sporadic contractions (↑ in the last 4-8 wks. Of pregnancy)	Regular intervals
Painless or mild intensity	Progressively ↑ in frequency and intensity
Not associated with progressive cervical dilation and effacement	Associated with cervical dilation
Resolve with rest, hydration, and/or sedation	Not resolve with sedation

3. What should you counsel the patient regarding the signs and symptoms of preterm labor?

The primary method for identifying preterm labor is by screening for maternal signs and symptoms as summarized below:

Menstrual-like cramps	Abdominal pressure
Pelvic pressure	Uterine contractions, often painless
Low, dull backache	Abdominal cramping (with or without diarrhea)
Increase or change in vaginal discharge (mucous, watery, light bloody discharge)	

4. What recommendations, if any, would you discuss with this patient regarding prevention strategies to reduce the risk of preterm delivery in this pregnancy? To reduce the risk of neurodevelopmental disorders and other morbidity associated with preterm labor in this fetus should she experience preterm labor?

- **Intramuscular or vaginal progesterone**, begun in the second trimester, has been shown to decrease the rate of preterm birth in women who previously experienced a preterm birth. Evidence does not currently exist to recommend one route of progesterone delivery over the other in preventing preterm delivery. Intramuscular or vaginal progesterone, begun in the second trimester.
- **Magnesium sulfate administered to the mother**, prior to an anticipated preterm birth, reduces the risk of cerebral palsy in surviving infants; thus, if delivery before 34 weeks gestation is anticipated, consideration should be given to administration of magnesium sulfate.
- **Antibiotics** should be administered during preterm labor as prophylaxis against Group B strep sepsis in the neonate.
- A course of **antenatal steroids** (betamethasone or dexamethasone) should be administered to the mother diagnosed with preterm labor in an effort to enhance fetal lung maturity and decrease the risk of necrotizing fasciitis and intracranial bleeds in the neonate.

5. If the patient does experience PTL in this pregnancy, what recommendations would you make regarding treatment and management?

- Fetal fibronectin testing (negative) and cervical length (greater than 2.5 cm) have good negative predictive value in deciding which patients do not require treatment for preterm labor.
- There is no clear first line tocolytic medication; however, current medications in use include magnesium sulfate, nifedipine, indomethacin, and beta-mimetics. The primary benefit of tocolytics appears to be delaying delivery in order to complete a course of antenatal steroids and transport the mother to a tertiary care facility for adequate care of the premature newborn.
- The risks of tocolytics include:

Magnesium:

- Maternal flushing, decreased reflexes, muscle weakness, pulmonary edema and fetal lethargy, hypotonia, respiratory distress and bone abnormalities if used > 7 days.

Nifedipine:

- Maternal hypotension.

Indomethacin:

- Maternal nausea, esophageal reflux, gastritis, emesis and possible platelet dysfunction and fetal in utero closure of ductus arteriosus with > 48 hour use and possibly patent ductus arteriosus for neonate.

Beta-mimetics:

- Maternal tachycardia, hypotension, tremor, shortness of breath, chest discomfort, pulmonary edema, hypokalemia and hyperglycemia and fetal tachycardia.

6. What are the potential adverse outcomes of preterm birth for the fetus?

Respiratory distress syndrome (RDS)	Intraventricular hemorrhage
Necrotizing enterocolitis	Sepsis
Neurologic impairment	Seizures
Long term-bronchopulmonary dysplasia	Developmental abnormalities: cerebral palsy