PRETERM LABOR

Ina S. Irabon, MD, FPOGS, FPSRM, FPSGE
Obstetrics and Gynecology
Reproductive Endocrinology and Infertility
Laparoscopy and Hysteroscopy

Doc Ina Ob Gyne

Doc Ina's lectures for Obstetrics and Gynecology topics

Reference

- Cunningham FG, Leveno KJ, Bloom SL, Spong CY, Dashe JS, Hoffman BL, Casey BM, Sheffield JS (eds). William's Obstetrics 24th edition; 2014; chapter 42 Preterm Labor

OUTLINE

- Definition
- Causes/ Contributing factors
- Diagnosis
- Prevention of preterm birth
- Management of Preterm prematurely ruptured membranes
- Management of Preterm labor with intact membranes
- Tocolysis

Definition

- **Preterm labor** – labor that commences < 37 weeks
  - Early Preterm: < 33 6/7 weeks
  - Late Preterm : 34 – 36 weeks
- **Low Birth weight**: < 2500 grams
- **Very Low birth weight**: <1500 grams
- **Extremely low birth weight**: <1000 grams
- **Preterm Premature Rupture of membranes (PPROM)**: spontaneous rupture of the fetal membranes before 37 completed weeks and before labor onset

Causes of Preterm labor/delivery

(1) spontaneous unexplained preterm labor with intact membranes
(2) idiopathic preterm premature rupture of membranes (PPROM)
(3) delivery for maternal or fetal indications
(4) twins and higher-order multifetal births.

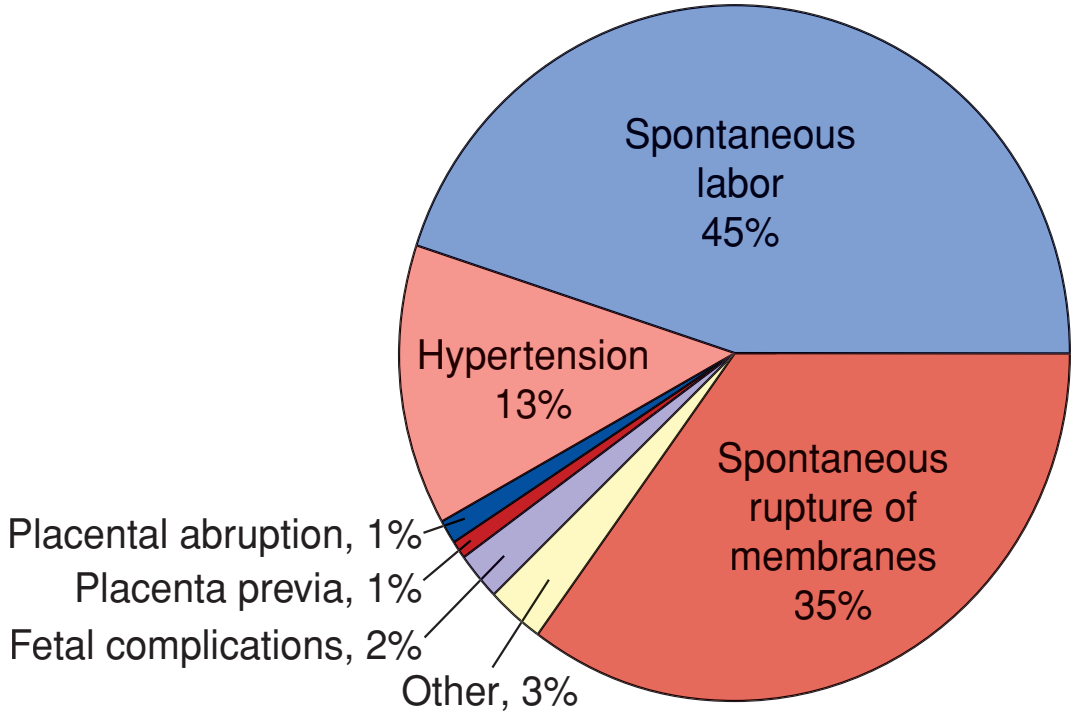

FIGURE 42-7 Obstetrical complications associated with 21,771 late preterm births at Parkland Hospital. (Adapted from McIntire, 2008.)

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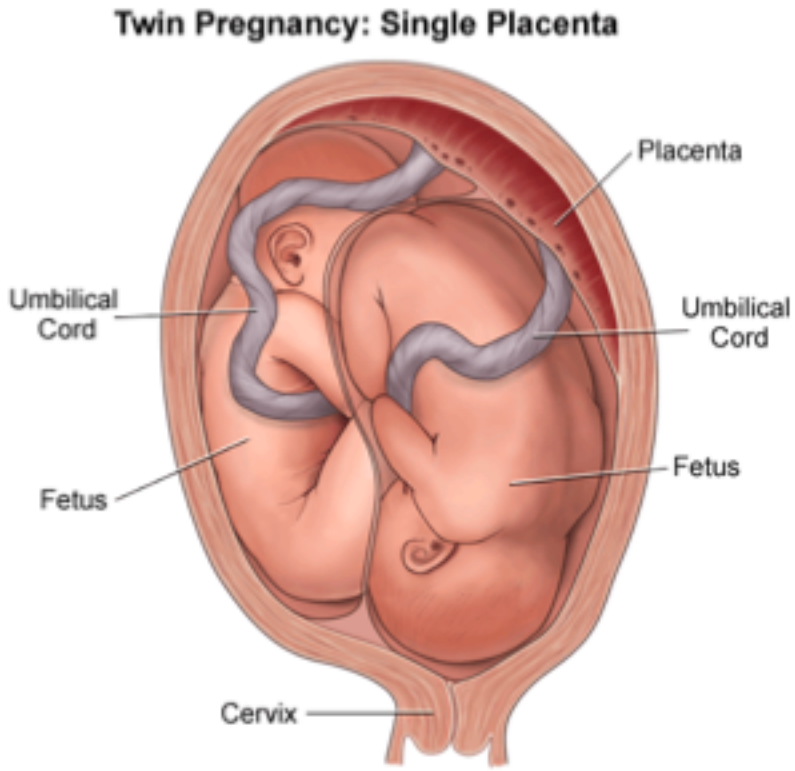
Causes of Preterm labor/delivery

1. Uterine distention

- multifetal pregnancy and hydramnios
- early uterine distention acts to initiate expression of contraction-associated proteins (CAPs) in the myometrium
- gastrin-releasing peptides (GRPs) are increased with stretch to promote myometrial contractility
- Excessive uterine stretch also leads to early activation of the placental–fetal endocrine cascade



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Causes of Preterm labor/delivery

2. Maternal-Fetal stress

- premature rise in cortisol and estrogens results in an early loss of uterine quiescence
- spontaneous preterm labor is associated with an early rise in maternal CRH levels and that CRH determination may be a useful biomarker for preterm birth risk assessment

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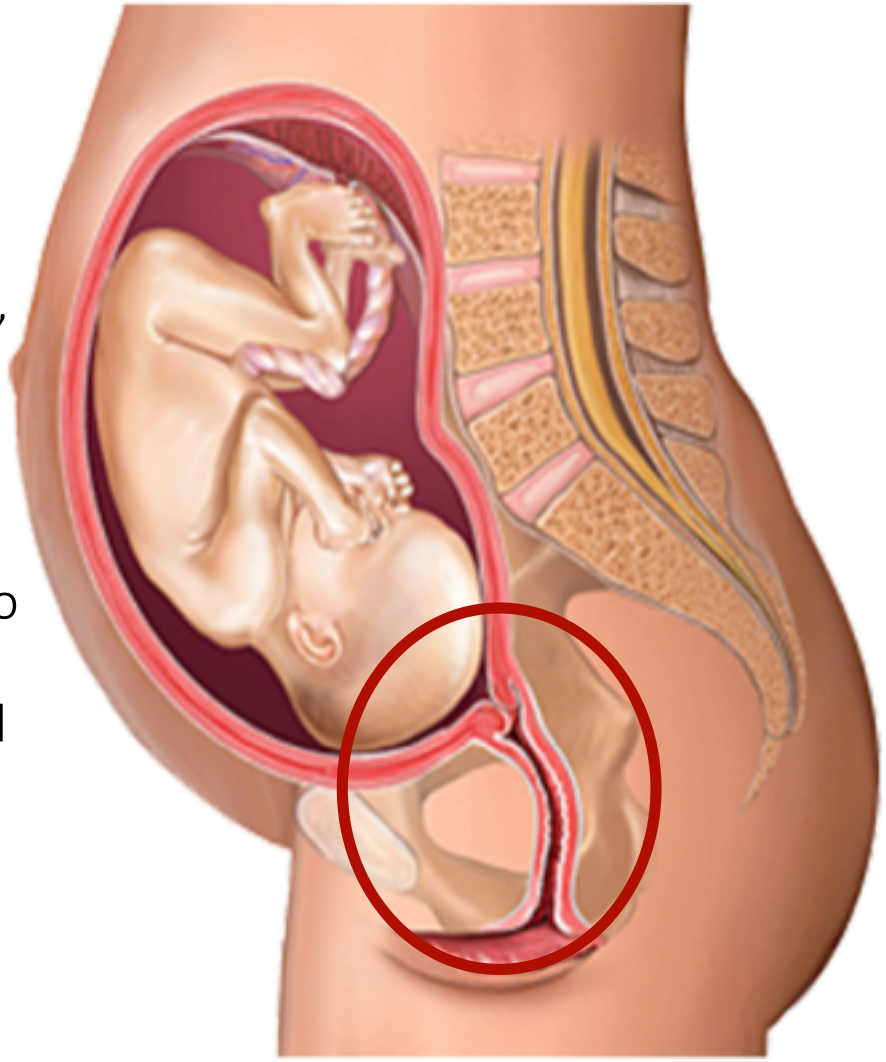
Causes of Preterm labor/delivery

3. Infection

- microbial invasion of the reproductive tract is sufficient to induce infection-mediated preterm birth—more specifically, there is ongoing "subclinical" infection.
- bacteria can gain access to intrauterine tissues through: (1) transplacental transfer of maternal systemic infection, (2) retrograde flow of infection into the peritoneal cavity via the fallopian tubes, or (3) ascending infection with bacteria from the vagina and cervix.
- *Gardnerella vaginalis*, *Fusobacterium*, *Mycoplasma hominis*, and *Ureaplasma urealyticum*



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Causes of Preterm labor/delivery

4. Lifestyle factors

- Cigarette smoking, inadequate maternal weight gain, socioeconomic status, and illicit drug use

5. Genetic Factors

6. Interval between Pregnancies

- Short intervals between pregnancies (intervals < 18 months) were associated with increased risks for both preterm birth and small-for- gestational age newborns

7. Prior preterm delivery

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Complications

TABLE 42-2. Major Short- and Long-Term Problems in Very-Low-Birthweight Infants

Organ or System	Short-Term Problems	Long-Term Problems
Pulmonary	Respiratory distress syndrome, air leak, bronchopulmonary dysplasia, apnea of prematurity	Bronchopulmonary dysplasia, reactive airway disease, asthma
Gastrointestinal or nutritional	Hyperbilirubinemia, feeding intolerance, necrotizing enterocolitis, growth failure	Failure to thrive, short-bowel syndrome, cholestasis
Immunological	Hospital-acquired infection, immune deficiency, perinatal infection	Respiratory syncytial virus infection, bronchiolitis
Central nervous system	Intraventricular hemorrhage, periventricular leukomalacia, hydrocephalus	Cerebral palsy, hydrocephalus, cerebral atrophy, neurodevelopmental delay, hearing loss
Ophthalmological	Retinopathy of prematurity	Blindness, retinal detachment, myopia, strabismus
Cardiovascular	Hypotension, patent ductus arteriosus, pulmonary hypertension	Pulmonary hypertension, hypertension in adulthood
Renal	Water and electrolyte imbalance, acid-base disturbances	Hypertension in adulthood
Hematological	Iatrogenic anemia, need for frequent transfusions, anemia of prematurity	
Endocrinological	Hypoglycemia, transiently low thyroxine levels, cortisol deficiency	Impaired glucose regulation, increased insulin resistance

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Complications

TABLE 42-5. Neonatal Morbidity Rates at Parkland Hospital in Live Births Delivered Late Preterm Compared with 39 Weeks

	Preterm Births			Term Births
Morbidity[a]	34 Weeks n = 3498	35 Weeks n = 6571	36 Weeks n = 11,702	39 Weeks n = 84,747
Respiratory distress				
Ventilator	116 (3.3)[b]	109 (1.7)[b]	89 (0.8)[b]	275 (0.3)
Transient tachypnea	85 (2.4)[b]	103 (1.6)[b]	130 (1.1)[b]	34 (0.4)
Intraventricular hemorrhage				
Grades 1, 2	16 (0.5)[b]	13 (0.2)[b]	7 (0.06)[c]	13 (0.01)
Grades 3, 4	0	1 (0.02)	1 (0.01)	3 (0.004)
Sepsis				
Evaluation	1073 (31)[b]	1443 (22)[b]	1792 (15)[b]	10,588 (12)
Culture proven	18 (0.5)[b]	23 (0.4)[b]	26 (0.2)[c]	97 (0.1)
Phototherapy	13 (6.1)[b]	227 (3.5)[b]	36 (2.0)[b]	857 (1)
Necrotizing enterocolitis	3 (0.09)[b]	1 (0.02)[c]	1 (0.001)	1 (0.001)
Apgar ≤ 3 at 5 min	5 (0.1)	12 (0.2)[b]	10 (0.9)	54 (0.06)
Intubation in delivery room	49 (1.4)[b]	55 (0.8)[c]	36 (0.6)	477 (0.6)
One or more of the above	1175 (34)[b]	1565 (24)[b]	1993 (17)[b]	11,513 (14)

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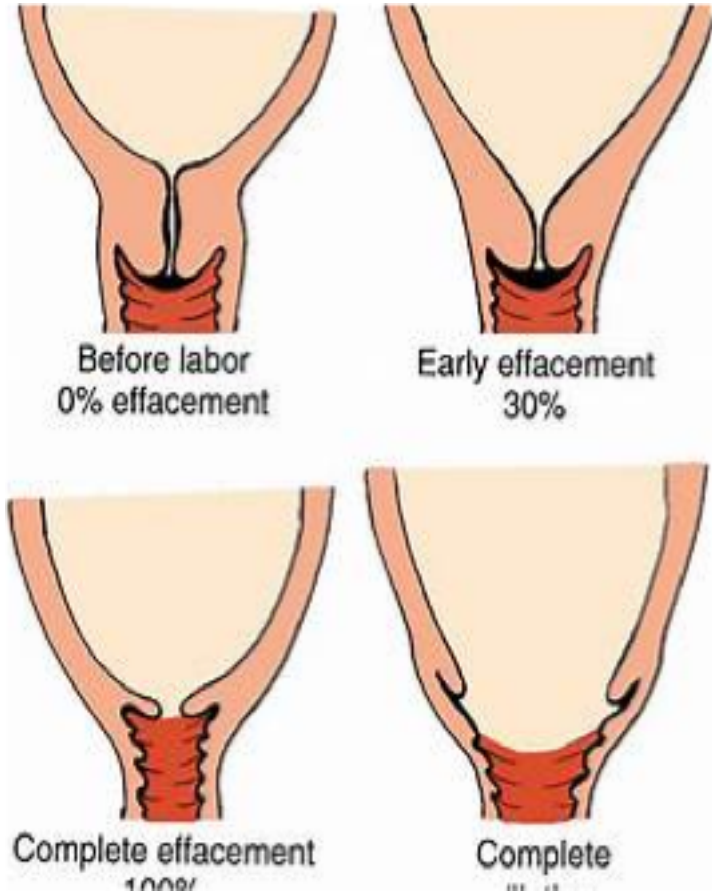
Diagnosis

- Preterm labor is primarily diagnosed by symptoms and physical examination. Sonography is used to identify asymptomatic cervical dilation and effacement.
- Symptoms:
  - painful or painless uterine contractions, symptoms such as pelvic pressure, menstrual-like cramps, watery vaginal discharge, and lower back pain
- Cervical changes
  - dilatation
  - effacement



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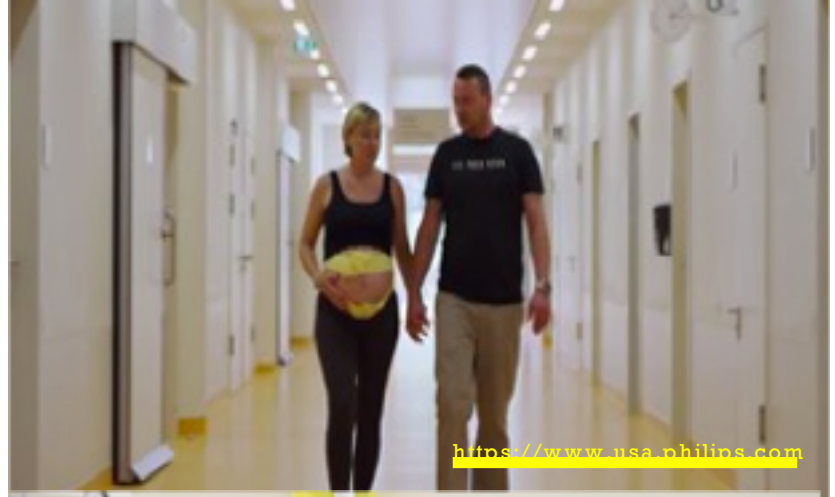
Diagnosis

- Ambulatory Uterine Monitoring
- Fetal Fibronectin
  - glycoprotein present in high concentrations in maternal blood and in amnionic fluid, it is thought to function in intercellular adhesion during implantation and in maintenance of placental adherence to uterine decidua
  - fibronectin detection in cervicovaginal secretions before membrane rupture was a possible marker for impending preterm labor.



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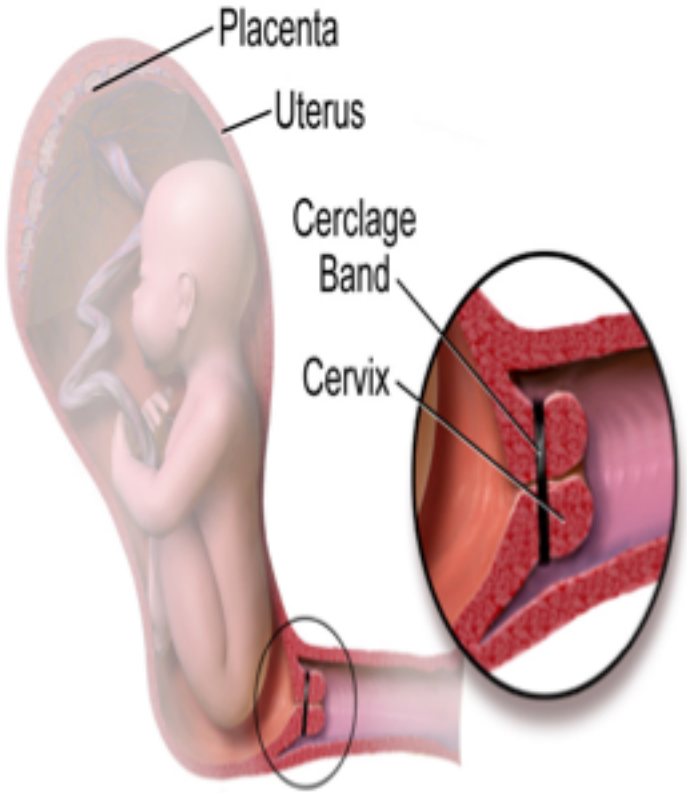
Preterm birth prevention

1. Cervical cerclage
   - prophylactic cerclage is used in women who have a history of recurrent midtrimester losses and who are diagnosed with cervical insufficiency
   - prophylactic cerclage for women identified during sonographic examination to have a short cervix.
   - "rescue" cerclage, done emergently when cervical incompetence is recognized in women with threatened preterm labor.



Cerclage Correction of the Cervix

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Preterm birth prevention

2.Prophylaxis with Progestin Compounds

- administration of progesterone to maintain uterine quiescence may block preterm labor.
  - Basis: human parturition involves functional proges- terone withdrawal mediated by decreased progesterone activity of progesterone receptors

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Diagnosis of PPROM

- history of vaginal leakage of fluid (either as a continuous stream or as a gush) should prompt a speculum examination to visualize gross vaginal pooling of amnionic fluid.
- Confirmation of ruptured membranes is usually done by:
  - sonographic examination to assess amnionic fluid volume
  - pH testing of cervicovaginal fluid: slightly alkaline (pH 7.1 – 7.3)

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Management of PPROM

- Hospitalization
  - most women enter labor within a week or less after membrane rupture.
  - Risk of cord prolapse
- Steroids
  - Betamethasone
  - Dexamethasone
- Intentional delivery vs expectant management

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Management of PPROM

- Antimicrobial Therapy
  - benefits: lower incidence of chorioamnionitis and fetal/newborn sepsis, pregnancy was more often prolonged approx. 7 days
  - Ampicillin, erythromycin (note: avoid amoxicilillin clavulanate due to increase incidence of necrotizing enterocolitis)

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Management of PPROM

TABLE 42-9. Recommended Management of Preterm Ruptured Membranes

Gestational Age	Management
34 weeks or more	Proceed to delivery, usually by induction of labor Group B streptococcal prophylaxis is recommended
32 weeks to 33 completed weeks	Expectant management unless fetal pulmonary maturity is documented Group B streptococcal prophylaxis is recommended Corticosteroids—no consensus, but some experts recommend Antimicrobials to prolong latency if no contraindications
24 weeks to 31 completed weeks	Expectant management Group B streptococcal prophylaxis is recommended Single-course corticosteroid use is recommended Tocolytics—no consensus Antimicrobials to prolong latency if no contraindications
Before 24 weeks[a]	Patient counseling Expectant management or induction of labor Group B streptococcal prophylaxis is not recommended Corticosteroids are not recommended Antimicrobials—there are incomplete data on use in prolonging latency

[a]The combination of birthweight, gestational age, and sex provides the best estimate of chances of survival and should be considered in individual cases.

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Risk of PPROM

- **Clinical Chorioamnionitis (intraamnionic infection)**
  - If chorioamnionitis is diagnosed, prompt efforts to effect delivery, preferably vaginally, are initiated.
  - higher incidence of sepsis, respiratory distress syndrome, early-onset seizures, intraventricular hemorrhage, and periventricular leukomalacia in the newborn.
  - Signs:
    - Fever: most reliable indicator (temperature of 38°C (100.4°F) or higher)
    - Maternal leukocytosis
    - sustained maternal or fetal tachycardia
    - uterine tenderness
    - malodorous vaginal discharge

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Management of Preterm labor with intact membranes

- If possible, delivery before 34 weeks is delayed.
- American College of Obstetricians and Gynecologists (2012a): single rescue course of antenatal corticosteroids should be considered in women before 34 weeks whose prior course was administered at least 7 days previously.
- Antimicrobials: antimicrobial treatment of women with preterm labor for the sole purpose of preventing delivery is generally not recommended.
- Bed rest: no evidence
- Cervical pessary: no evidence
- Cerclage: may possibly be useful in delaying delivery.

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Tocolysis to Treat Preterm Labor

- the American College of Obstetricians and Gynecologists (2012a) has concluded that tocolytic agents do not markedly prolong gestation but may delay delivery in some women for up to **48 hours** → this may allow transport to a regional obstetrical center and permit time for corticosteroid therapy.
- **Beta-adrenergic agonists, calcium-channel blockers, or indomethacin** are the recommended tocolytic agents for such short-term use—up to 48 hours.
- In general, if tocolytics are given, they should be adminis- tered concomitantly with corticosteroids.

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Tocolytic agents: β-Adrenergic Receptor Agonists

- Several compounds react with β-adrenergic receptors to reduce intracellular ionized calcium levels and prevent activation of myometrial contractile proteins
- In the United States, ritodrine and terbutaline have been used in obstetrics, but only ritodrine had been approved for preterm labor by the FDA.

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Tocolytic agents: β-Adrenergic Receptor Agonists

- Ritodrine: voluntarily withdrawn from the United States market in 2003.
- The brief delay in delivery (approx 48h) may aid maternal transport to tertiary care or permit fetal lung maturation with corticosteroids.
- Possible maternal side effects: pulmonary edema, acute respiratory distress, volume overload (retention of sodium and water), increased capillary permeability, cardiac rhythm disturbances, and myocardial ischemia.

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Tocolytic agents: β-Adrenergic Receptor Agonists

- Terbutaline: IV or oral
- can also cause pulmonary edema. In 2011, the FDA issued a warning regarding use of terbutaline to treat preterm labor because of reports of serious maternal side effects.

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Tocolytic agents: Magnesium Sulfate

- Ionic magnesium in a sufficiently high concentration can alter myometrial contractility.
- Acts as a calcium antagonist, and thus, it may inhibit labor.
- intravenous magnesium sulfate—a 4-g loading dose followed by a continuous infusion of 2 g/hr—usually arrests labor.
- FDA (2013) warned against prolonged use of magnesium sulfate given to arrest preterm labor due to bone thinning and fractures in fetuses exposed for more than 5 to 7 days → attributed to low calcium levels in the fetus.
- has a fetal neuroprotective effect (very-low-birthweight neonates whose mothers were treated with magnesium sulfate for preterm labor or preeclampsia were found to have a reduced incidence of cerebral palsy at 3 years)

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Tocolytic agents: Prostaglandin Inhibitors

- Prostaglandins are intimately involved in contractions of normal labor
- Antagonists act by inhibiting prostaglandin synthesis or by blocking their action on target organs.
- A group of enzymes collectively termed prostaglandin synthase is responsible for the conversion of free arachidonic acid to prostaglandins Several drugs block this system, including acetylsalicylate and indomethacin.
- Indomethacin is administered orally or rectally: dose of 50 to 100 mg is followed at 8-hour intervals not to exceed a total 24-hour dose of 200 mg.
- indomethacin use is limited to 24 to 48 hours because of concerns for oligohydramnios → reversible with drug discontinuation.

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Tocolytic agents: Calcium-Channel Blockers

- Calcium-channel blockers act to inhibit, by various mechanisms, calcium entry through cell membrane channels.
- the combination of nifedipine with magnesium for tocolysis is potentially dangerous: Nifedipine enhances the neuromuscular blocking effects of magnesium that can interfere with pulmonary and cardiac function.

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Tocolytic agents: Atosiban and Nitric Oxide Donors

- Atosiban
  - This nonapeptide oxytocin analogue is a competitive antagonist of oxytocin-induced contractions.
- Nitric Oxide Donors
  - these potent smooth-muscle relaxants affect the vasculature, gut, and uterus.
  - maternal hypotension was a common side effect

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SUMMARY

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Thank you!

youtube channel: Ina Irabon

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