CHAPTER 15
PRETERM LABOUR AND PRETERM BIRTH

Learning Objectives
By the end of this chapter, the participant will:

1. Define preterm labour and recognize its significance to infant mortality and morbidity.
2. Describe the common causes of preterm labour.
3. Describe the criteria used to diagnose preterm labour.
4. Explain the management of preterm labour and preterm birth.

Definition

Preterm labour (PTL) is defined as regular uterine contractions accompanied by progressive cervical dilation and/or effacement at less than 37 weeks. Long-term adverse sequelae of preterm birth (PTB) occur mainly in those born at less than 34 weeks gestational age. Significant morbidity and mortality occurs particularly in those born at less than 30 weeks gestational age. Clinically significant PTB applies to birth where a delay would produce a decrease in neonatal morbidity or mortality. Practically speaking, this applies to births that occur before 34 weeks gestation.

Incidence and Significance

PTB occurs in about 7% to 10% of pregnancies. In a developed country such as Canada, the incidence has not changed significantly in the past 30 years. Only about 1% to 2% of pregnancies deliver before 34 weeks. Neonates born at greater than 34 weeks gestational age in tertiary centres have survival rates equal to those born at term, although they may require longer hospital stays due to feeding and other minor difficulties.

The importance of accurate dating cannot be overstated in the management of PTL. A difference of 10 days can change the chance of survival from near zero to 30% or from 30% to 55%. For this reason, accurate dates must be established, and the estimated date of delivery must be communicated effectively to the patient. By 20 weeks gestation, all women should know their estimated date of delivery from accurate menstrual data or dating from an ultrasound where available.

Where facilities exist, it is recommended that all women be offered a routine ultrasound at 18 to 20 weeks. This ultrasound will confirm menstrual-based gestational age. For women who do not have good menstrual data, an early ultrasound is recommended to establish the estimated date of delivery. A crown–rump length at 8 to 12 weeks will predict the expected date of birth to within 5 days (2 standard deviations).

Seventy-five percent (75%) of neonatal mortality occurs in infants born preterm. The long-term sequelae of PTB include:

- Central nervous system complications, such as cerebral palsy
- Neurodevelopmental delay
- Respiratory complications, such as bronchopulmonary dysplasia
- Blindness and deafness

The above complications have their highest incidence in births occurring at less than 30 weeks gestation.

Mother-to-child-transmission of HIV is increased with premature delivery, possibly due to association with other infections and the immature immune system of the fetus.

Physical, psychological, and financial burdens associated with the diagnosis, management, and outcome of preterm labour and delivery are significant.

Etiology
Preterm delivery may be secondary to:

1. Preterm premature rupture of membranes (30% to 40% of preterm births)
2. Spontaneous PTL with intact membranes (40% to 50% of preterm births)
3. Indications (20% to 28% of PTBs)[1,2]

The most common indications for a PTB include:
- Gestational hypertension
- Abnormal fetal monitoring findings
- Intrauterine growth restriction
- Placental abruption, often occult (i.e. hidden)
- Intrauterine demise
- Chorioamnionitis

Risk Assessment for Preterm Labour and Preterm Birth
- History of spontaneous PTB
- Preterm pre-labour rupture of membranes in current pregnancy
- Antepartum hemorrhage
- Uterine overdistension due to multifetal gestation or polyhydramnios
- Incompetent cervix or uterine anomaly (uterine abnormality)
- Fetal anomaly
- Second trimester bleeding
- Infection
  - Chorioamnionitis
  - Bacteriuria
  - Periodontal disease
  - Current bacterial vaginosis with a prior PTB
- Drugs, smoking (e.g. smoking >10 cigarettes/day), lifestyle, stress
- Domestic violence
- Demographic factors:
  - Maternal age <18 years and >35 years
  - Maternal weight <55 kg

Interventions

Where laboratory facilities exist, screening for and treating bacterial vaginosis in a woman who has had a prior PTB has been shown to reduce the risk of low birth weight (OR, 0.31; 95% CI, 0.13–0.75) and preterm pre-labour rupture of membranes (OR, 0.14; 95% CI, 0.05–0.38).[3]

Screening for and treating asymptomatic bacteriuria has been shown to reduce preterm delivery or low birth weight (OR, 0.60: CI, 0.45–0.80).[4]

Bed rest, avoiding coitus, and home uterine monitoring have **not** been shown to decrease the PTB rate in randomized controlled trials.

Diagnostic Strategies

1. Early diagnosis
   - Women should be instructed early in their antepartum care to be vigilant for signs and symptoms of impending PTL and to contact their health care provider or go to their health care facility. Signs and symptoms may include:
     - Contractions
     - Vaginal fluid loss
     - Vaginal bleeding
     - Maternal perception of changes in pelvic pressure, low dull backache, or vaginal discharge
2. In the presence of worrisome signs and symptoms, women should be encouraged to report to their health care provider, health centre, or local hospital immediately.
3. Timely physical assessment to confirm PTL

Clinical suspicion should be raised by the presence of uterine contractions combined with a cervical examination suggesting early dilation and/or effacement. This approach facilitates early institution of therapy but results in a 50% over-diagnosis of PTL.

Management of Preterm Labour

To ensure appropriate management of PTL, every health care provider should have the skills to:
- Identify the cause of PTL and treat the underlying cause, when possible
- Attempt to arrest or stop labour when appropriate
- Intervene to minimize neonatal morbidity and mortality

Assessment

Establish dates
- Review history of pregnancy with the woman (estimated date of delivery , menstrual history, ultrasounds)
- Examine the prenatal record for menstrual history, estimated date of delivery, information from dating ultrasound, and clinical growth

Evaluate contractions
- History (frequency, intensity, duration, changes with time)
- Abdominal examination for uterine activity
- Tocodynamometer, if available

Cervical assessment
- Sterile speculum exam initially to rule out preterm pre-labour rupture of membranes (PPROM) and to obtain cultures, if indicated
- Digital examination after prerupture of membranes ruled out to determine position, dilation and effacement

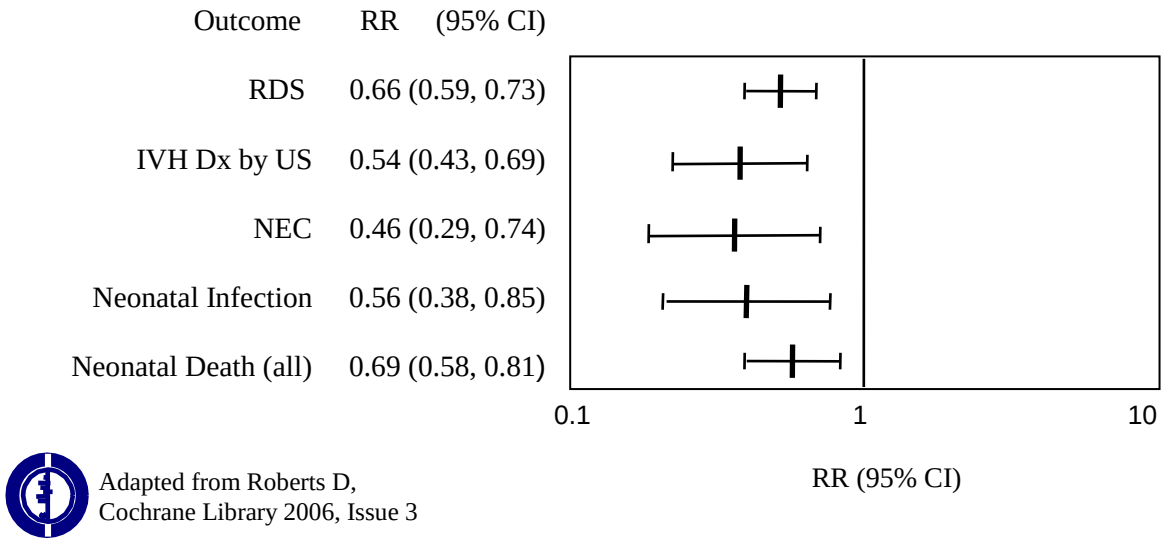
Prolongation of Pregnancy

No intervention has been shown to reduce the incidence of PTB. However, tocolysis has been shown to prolong pregnancy for 48 hours or more. This provides the window of opportunity for the administration and absorption of glucocorticoids. It also allows for the transportation of the woman to a tertiary centre if necessary. In a significant percentage of women in PTL, tocolysis may be contraindicated.

Antenatal glucocorticoid therapy

The benefits of antenatal glucocorticoid therapy are now definitively established. Betamethasone and dexamethasone cross the placenta and induce enzymes that accelerate fetal pulmonary maturity. It takes 48 hours after the first dose for the full benefit to be achieved. An incomplete course of steroid therapy may still offer worthwhile benefits. The graph below shows the meta-analysis of steroids in PTL.[5] Both betamethasone and dexamethasone have been shown to reduce respiratory distress syndrome (RDS) and intraventricular hemorrhage. Betamethasone, but not dexamethasone, has been shown to reduce cystic periventricular leukomalacia and perinatal mortality overall.

Figure 1 - Antenatal steroids versus no treatment[a]



Adapted from Roberts D, Cochrane Library 2006, Issue 3

Recommendations for antenatal steroids

Everyone who is at increased risk of a preterm delivery is a candidate for antenatal steroid therapy.

When should steroid therapy be given?

- Lower gestation limit viability
- Upper gestational limit is 34 weeks
- Prophylactic administration depends on diagnosis and risk
- Repeated administration use restricted to ongoing clinical trials

Steroid options

- Betamethasone l2mg IM q 24h H 2 doses (preferred)
- Dexamethasone 6mg IM q 12h H 4 doses

[a] **Abbreviations used in figure 1**: RR = relative risk, CI = confidence interval, RDS = respiratory distress syndrome, IVH = intraventricular hemorrhage, Dx = diagnosis, NEC = necrotizing enterocolitis

Caution with the use of steroids

- If immediate delivery is indicated, do not delay to wait for steroid effect
- Will increase the maternal blood sugar in women with diabetes
- Will increase the white blood cells
- Caution should be used when corticosteroids are given in the presence of cardiac disease, active tuberculosis, gastric ulcers, chorioamnionitis and placental abruption

Tocolytics with Evidence for Some Efficacy

- **Calcium channel blockers (nifedipine)**
  - No placebo controlled trials
  - The Cochrane Database of Systematic Reviews 2003, Issue 1)
    - Twelve trials (n=1029) comparing nifedipine with another tocolytic (mainly betamimetics)
      - lower rate of delivery within 7 days and <34 weeks, reduced rates of RDS, necrotizing enterocolitis, intraventricular hemorrhage, and jaundice with nifedipine (These significant findings are driven mainly by one study finding significant differences.[6]
      - fewer side effects and hence less need to discontinue treatment
  - Dose: Ideal dosage regimen not yet determined, but many centres in Canada are using this as their first line tocolytic. Typical regimens include a loading dose of 10 mg to 30 mg with repeat doses of 10 mg to 20 mg if contractions continue.
  - Side effects: Generally well tolerated, but may cause maternal dizziness, lightheadedness, headache, flushing, nausea, and transient hypotension
- **Prostaglandin synthetase inhibitors (indomethacin)**
  - Cochrane Database of Systematic Reviews 2005, Issue 215
    - Three small trials (n=106) compared with placebo:
      - more effective than placebo in delaying delivery to $\geq$37 weeks (This finding is based on only one small study.)
    - Five trials compared with other tocolytics:
  - More effective in delaying delivery to >37 weeks and decrease in maternal drug reaction requiring cessation of treatment
  - Consult local tertiary centre as to local standard of care
  - Dose: 100 mg suppository for transport and repeat 25 mg to 50 mg q 6 hours for a maximum of 48 hrs
- **Fetal complications**
  - Should not be used after 32 weeks gestation because of increased sensitivity of the ductus arteriosus to closure
  - Reduced fetal urine production causing oligohydramnios; neonatal renal insufficiency has been reported.
- **Oxytocin antagonists (Atosiban)**
  - Not approved by Health Canada or US Food and Drug Administration but available in Europe
  - Cochrane Database of Systematic Reviews 2005, Issue 316
    - Two trials compared with placebo (n=613)
      - Atosiban resulted in lower infant birth weight and more maternal adverse drug reactions.
    - Four trials (n=1035) compared with betamimetics:
      - Atosiban increased the numbers of infants born under 1500 grams and fewer maternal drug reactions requiring treatment cessation.
  - The use of Atosiban is not supported and the increase in infant deaths is of concern.
- **β adrenergic agonists (ritodrine, terbutaline)**
  - Ritodrine and terbutaline are not approved for obstetric use in Canada.
  - Cochrane Database of Systematic Reviews 2004, Issue 417
    - Eleven trials compared with placebo (n=1332)
      - more effective than placebo in delaying delivery by at least 48 hours
      - significant maternal side effects including chest pain; dyspnea; tachycardia; palpitation; tremor; headaches; hypokalemia; hyperglycemia; nausea/vomiting; and nasal stuffiness

Tocolytics with No Evidence for Efficacy

- **Magnesium sulphate**
  - Cochrane Database of Systematic Reviews 2002, Issue 418
    Three trials compared with placebo, 20 trials compared with other tocolytics (many poor quality studies)
    - **no benefit** at any dose as a tocolytic
- Progesterone
    - Progesterone is **NOT** a tocolytic and is **NOT** effective as a tocolytic.
    - Progesterone has been used to prevent PTL in women with a history of PTL and PTB. There is a multi-centre trial taking place now in Canada to determine if it is effective used in this situation.

Contraindications to Tocolysis

- Any contraindications to continuing the pregnancy
  - Gestational hypertension with proteinuria or other medical indication
  - Chorioamnionitis
  - Mature fetus
  - Imminent delivery
  - Intrauterine fetal death or lethal fetal abnormality
- Contraindications to specific tocolytic agents

For the following interventions, there is no evidence of any benefit. However, there may not have been sufficient studies to evaluate the effectiveness of some of these interventions:

- Bed rest
- Fluid bolus
- Sedation, narcotics
- Home uterine activity monitoring

Minimizing Neonatal Morbidity and Mortality

Respiratory distress syndrome is a major concern with preterm delivery. Intraventricular hemorrhage, necrotising enterocolitis, persistent pulmonary hypertension and other respiratory conditions are also associated with PTB and are more likely to occur in newborns with RDS. In the past, RDS accounted for more than one-fifth of all neonatal deaths. The increased use of antenatal steroids and innovations in neonatal care has reduced its occurrence.

Maternal transport

The decision to transport should be made in consultation with the receiving health care provider. Where possible, a birth attendant should accompany the woman. Family members should also accompany the woman.

Consider

- Availability of neonatal and obstetrical care
- Availability of transport and skilled personnel
- Travel time
- Stability of the woman and her fetus
- Risk of delivery en route
  - parity, length of previous labour
  - cervical status
  - contractions: response to tocolytics, if administered
  - presentation of fetus

Transport plan

Every health care facility should have a transport protocol that includes:

- Copies of antenatal forms, lab results, ultrasound reports
- Guidelines for communication
  - with patient and family
  - with receiving physician re indication, stabilization, mode of transport, and estimated time of arrival
- Provision for an appropriate skilled birth attendant for transport
- Provision for IV access, indicated medications, and appropriate equipment to be sent with the woman
- Assessment of patient immediately prior to transport

These issues are detailed in the Society of Obstetricians and Gynaecologists of Canada's *Maternal Fetal Transport Guidelines*: http://www.sogc.org/guidelines/public/165E-PS-October2005.pdf

Location of preterm birth

It has been clearly shown that preterm infants born in tertiary-care (level III) centres, hospitals with neonatal intensive care facilities experience less mortality and long-term morbidity than those born in other settings.

Best:	Level III Hospital with neonatal intensive care unit
	Level II Hospital
	Level I Hospital
Worst:	During Transport

Summary

- Diagnose promptly and accurately.
- Identify and treat underlying cause if possible.
- Attempt to prolong pregnancy if indicated to permit administration of steroid therapy.
- Intervene to minimize neonatal morbidity and mortality.
  - If resources are available, use the mnemonic STAT to remember the most appropriate management plan:
    - Steroids: Antenatal steroid therapy
    - Tocolytics: If indicated
    - Antibiotics: GBS (group B streptococcus) prophylaxis
    - Transport Assessment prior to transportation and availability of a skilled attendant

Other tools to predict a preterm delivery

- Fetal fibronectin

  Fetal fibronectin is a glycoprotein whose presence in cervicovaginal secretions before 34 weeks gestation is associated with PTL and PTB. Its main benefit has been shown to be its negative predictive value. A negative fetal fibronectin indicates a low probability of delivery within 7 to 14 days, even in the presence of contractions. The chance of delivering within 14 days of a negative fetal fibronectin (in women with symptoms) is 1% to 5%. The chance of delivering within 14 days with a positive test in women with symptoms is 17% to 41% (the positive predictive value). In a recent Canadian study of symptomatic women, it was found that a negative fetal fibronectin result conferred a 97.4% chance of not delivering within 7 days.[7]

  Fetal fibronectin testing is currently being advocated in some Canadian centres to assist in the diagnosis of PTL. The hope is that such testing will result in a decrease in unnecessary hospital admissions, transports, and potential treatment with steroids and tocolytics.

  Routine screening for fetal fibronectin is NOT advised. It may be a valuable screening tool when women are reporting signs and symptoms of PTL such as contraction or increased vaginal discharge.

- Cervical length measured by transvaginal sonography

  Cervical length has a normal distribution throughout gestation. The mean length at 24 to 28 weeks gestation is approximately 35 mm.

  The probability of PTB increases when the cervical length is <30 mm, especially in women at increased risk of PTB (e.g., those with a history of PTB). Funneling of the internal cervical os may be seen on ultrasound imaging, but is only significant when the residual cervical length is short. Transvaginal ultrasound imaging is preferred because transabdominal scanning requires some urine in the maternal bladder that may affect the cervical length (Iams, 2003).

Key Messages

1. Accurate diagnosis of PTL is difficult. Using risk factors to identify a woman in PTL may sometimes assist in the diagnosis, but it cannot predict PTL.
2. When PTL is suspected, tocolysis is appropriate to allow the administration of steroid therapy to improve neonatal mortality and morbidity.

Suggestion for Applying the Sexual and Reproductive Rights Approach to this Chapter

Having a preterm baby can be quite stressful for new parents. Ensure that the mother and her baby stay together by promoting "kangaroo care"*. Not only does this keep the baby warm but is also helps to alleviate the stress of delivering a small baby and creates a good start for building attachment or closeness to the new baby. Some mothers need lots of support. All mothers should be encouraged to give their baby breast milk even if the baby is too immature to suck. Cup feeding breast milk is a feeding option that should be promoted.

**Kangaroo care* is a way of holding a preterm baby so that there is skin-to-skin contact between the baby and the person holding it. The baby is naked or wearing only a diaper, is held against the parent's bare chest.

Resources:

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