INTRODUCTION

DEFINITION OF PRETERM LABOUR

Preterm labour is defined as regular uterine contractions with associated cervical changes at less than 37 weeks gestation.

Any signs and symptoms of preterm labor should be documented together with the duration of these symptoms. Symptoms may include abdominal cramps (with or without diarrhea), vaginal bleeding, ruptured membranes, increase in low back pain, pressure sensation in pelvis/vagina, change in vaginal discharge.

POLICY

General practitioners and midwives are expected to obtain consultation from a specialist obstetrician in the event of preterm labor in a patient who is less than 36 weeks gestation or premature rupture of membranes at less than 36 weeks gestation.

MANAGEMENT OF THREATENED PRETERM LABOUR

A. TELEPHONE ADVICE

If a woman experiencing signs or symptoms of threatened preterm labour contacts the Labor unit by telephone, she may be given the following advice:

- Lie down on left side and rest for one hour.
- Consider rehydration if patient's fluid intake has been decreased.
- If the symptoms go away after one hour, she may then begin light activity and inform her health care provider at the next prenatal visit.
- If the symptoms do not go away after one hour of rest, or if they return, she should call her physician.
- She should be advised to go immediately to the hospital:
  - if the symptoms get worse during the one hour rest;
  - if vaginal bleeding or fluid leak is present;
  - if she feels pelvic pressure or notes a change in her vaginal discharge;
  - if she is concerned or anxious about what is happening.
B. **PRESENTATION TO THE LABOUR & DELIVERY UNIT**

- Initial assessment may include the steps noted above under Telephone Advice.
- Ascertain duration, frequency and strength of contractions.
- Monitor fetal heart rate activity with continuous electronic fetal monitoring for minimum of 20 minutes.
- Physician should obtain fetal fibronectin or ACTIM PTL sample (pending introduction of clinical trial outcome).
- Sample for GBS culture should be obtained.
- Physician should then perform digital pelvic exam.
- Decide on plan of management ie: observation vs. tocolytic therapy (Appendix A - Decision Tree)
- All pregnancies between 23 and 33 completed weeks should receive Betamethasone.

Pelvic digital examination should not be performed until the appropriate samples have been obtained, ie: cultures, fetal fibronectin or ACTUM plus (pending introduction of clinical trial outcome). Digital examination should not be performed in the presence of active vaginal bleeding, unknown placental location or ruptured membranes unless directed by attending physician.

Decisions regarding observation vs. tocolysis depend on the following factors:

- Gestational age
- Cervical dilation
- Frequency and intensity of contractions
- Other fetal and maternal concerns

**TOCOLYSIS FOR PREVENTION OF PRETERM BIRTH**

**PURPOSE**

1. Tocolytic therapy has been shown to prolong pregnancy to provide benefit of administering antenatal glucocorticoids for fetal lung maturity.

2. Tocolytic therapy may play a role in the safe transportation of the mother diagnosed with preterm labor to the tertiary care facility.

**CLINICAL PRACTICE GUIDELINES**

1. Tocolytic therapy should only be considered between 23 and 33 completed weeks gestational age.

2. Tocolytic therapy should be considered only within the overall clinical context. Maternal and fetal complications should be taken into consideration.

3. There is no good evidence that tocolytic therapy is successful in the presence of multiple gestation, ruptured membranes, or with cervical dilation >4 cm. However, in these circumstances, tocolytic therapy may help delay delivery to maximize the benefit from glucocorticoid therapy.

4. There is no evidence to support prolonged tocolytic therapy (>48 hours).

5. The Neonatology team should be notified as far in advance as possible if preterm delivery is considered likely. A consult to Perinatology may be considered.
GENERAL CONTRAINDICATIONS TO TOCOLYSIS

1. Inappropriate gestational age, i.e. <23 weeks or >34 weeks gestation.

2. Internal medical disease, such as:
   - severe gestational hypertension
   - uncontrolled diabetes mellitus
   - cardiac disease (recent myocardial infarction, pulmonary hypertension, tachyarrhythmia)
   - chorioamnionitis
   - Use with caution in patients with impaired renal circulation.

3. Active antepartum hemorrhage.

4. Fetal complications:
   - intrauterine fetal demise or non-viable condition
   - fetal compromise (which may include fetal anomalies and/or suspected intrauterine growth restriction)
   - non-reassuring fetal assessment.

5. Known allergy to the tocolytic agent chosen.

TOCOLYTIC AGENTS

A variety of tocolytic agents that have been used or are being studied:

- Prostaglandin synthesis inhibitors (Indomethacin, Naproxen) – Appendix B
- Calcium channel blockers (Nifedipine, Nicardipine)
- Nitroglycerin – Appendix C

All of the above have potential maternal and fetal side effects. They should be used when the perceived benefit outweighs the risk.

Steroids

- Betamethasone (Appendix D)
APPENDIX A

PRETERM LABOR DECISION TREE

23 to 33 weeks GA in threatened preterm labour

Fetal Fibronectin / ACTIM PTL

Betamethasone

Swab GBS

Cervix not dilated

Observe

Consider Tocolysis

Cervix dilated

Nitroglycerin Study
Transfer to RAH

Indomethacin
Observe

Indomethacin
Transfer to RAH
APPENDIX B

INDOMETHACIN
ADMINISTRATION PROTOCOL

PHARMACOLOGY

Indomethacin is a non-steroidal anti-inflammatory that acts by inhibition of prostaglandin synthesis. It is completely absorbed after oral or rectal administration. Peak serum levels are seen within 2 hours of administration; the half-life is 3-11 hours.

PRECAUTIONS

- There is rapid and complete transfer of the drug to the fetus.
- Indomethacin, with prolonged therapy, may cause constriction of the fetal ductus arteriosus.
- Therapy longer than 48 hours may cause oligohydramnios and platelet dysfunction, and has been associated with an increase in the incidence of neonatal pulmonary hypertension, persistent ductus arteriosus, intraventricular hemorrhage, and necrotizing enterocolitis.

CONTRAINDICATIONS

A. Maternal

- pre-existing gastrointestinal lesions (ulcers)
- known allergies to NSAIDS or salicylates
- coagulation disorders or thrombolytic therapy
- renal or hepatic dysfunction

B. Fetal

- ≥32 weeks gestation
- pre-existing oligohydramnios
- fetal compromise, including IUGR, and fetal anomalies

Note: Refer also to “General Contraindications to Tocolysis” on page 3.

SIDE EFFECTS:

A. Maternal

- nausea
- heartburn
- headache
- vertigo
- tinnitus
- psychotic episodes
- pulmonary edema
B. **Fetal**
   - early constriction/closure of the ductus arteriosus
   - transient renal insufficiency
   - platelet dysfunction until drug excreted (seen more in neonates)

**PROTOCOLS**

1. The physician will assess the patient for premature labour and explain the need for and action of drug to patient and family.

2. The physician will provide written orders specifying dose, route, time of administration and required lab work, e.g.:
   - CBC, ultrasound/fetal assessment for amniotic fluid volume, including Doppler flow study
   - Indomethacin 100 mg pr q12h
     - Maximum of 4 doses
     - Maximum length of treatment is 48 hours
     - If used for greater than 72 hours, must be able to perform obstetrical ultrasound and Doppler flow.
     - Study to assess patency of the fetal ductus arteriosus.
     - Consultation to Perinatology must be obtained if treatment with Indomethacin has been or is being considered for greater than 72 hours.

**REFERENCES**


APPENDIX C

NITROGLYCERIN

The use of nitroglycerin in various forms (transdermal patch, IV bolus or infusion, nasal spray, sublingual) is being tested widely as a tocolytic agent for obstetrical emergencies. The Capital Health Region is currently participating in the Canadian Preterm Labour Nitroglycerin (GTN) Trial to evaluate the efficacy of nitroglycerin transdermal patch for preterm labour, and this protocol is based on that study protocol. To be included in this study, patient should not have been administered any other form of tocolytic. Administration of steroids and antibiotics is not an exclusion criteria. If using this form of tocolysis, the patient will require transfer to the RAH for inclusion within this study protocol. At this time, nitroglycerin should not be used for preterm labor outside of the study protocol. If considering transfer for the purpose of enrollment in this study, consideration should be given to obtaining consent prior to transfer.

PHARMACOLOGY

Nitroglycerin, a nitric oxide donor, is a potent endogenous smooth muscle relaxant. It is used as a uterine relaxant for other obstetrical situations, e.g. external cephalic version, removal of retained placenta.

POTENTIAL SIDE EFFECTS

- maternal hypotension
- headache
- fetal tachycardia
- fetal/neonatal hypotension

STUDY PROTOCOL

A. INCLUSION CRITERIA

- 24 to 32 weeks gestational age
- at least 4 contractions per 20 minutes; AND
- cervical change (change in Bishop Score or Bishop Score >6)

B. EXCLUSION CRITERIA

- Any maternal or fetal condition necessitating immediate delivery
- Multiple gestation
- Preeclampsia
- Intrauterine fetal demise or lethal fetal anomalies
- Cervical dilation >8 cm
- Treatment with another tocolytic agent within 24 hours
- Previous enrollment in this trial
- Known sensitivity to nitroglycerin
- Failure to give consent.
C. **METHOD**

   1. Examine and assess cervical length, effacement and dilation and calculate Bishop Score.
   2. Start IV bolus (NS or RL) to infuse over 30-60 minutes as prophylaxis against possibility of GTN-induced maternal hypotension.
   3. Repeat cervical exam following completion of IV bolus (30-60 minutes) to assess for change (i.e. Bishop Score increase compared to initial assessment).
   4. If woman is eligible for (i.e. meets inclusion/exclusion criteria) and has agreed to participate in the study (informed consent to be signed), she will be randomized to receive either transdermal GTN (0.4 mg/h) or placebo patch.
   5. Administer corticosteroid – Betamethasone (refer to protocol).

Refer to actual Study Protocol for complete instructions.

D. **MONITORING:**

   1. Continuous monitoring of fetal heart rate during the first 4 hours of treatment, and then intermittently at the discretion of the attending physician.
   2. Monitor maternal BP q15 min. x 1 hour, q30-60 min. x 4 hours, then q4h thereafter.
APPENDIX D

ANTENATAL GLUCOCORTICOIDS FOR FETAL MATURATION

INTRODUCTION

Glucocorticoid therapy reduces the frequency of respiratory distress syndrome (RDS), intraventricular hemorrhage (IVH) and neonatal mortality in infants weighing less than 2500 gm. In 1994 the National Institutes of Health (NIH) in the US concluded that antenatal glucocorticoids decrease the incidence of RDS in infants born 29 to 34 weeks gestation and reduce the severity of RDS in 24 to 28 weeks gestation. Glucocorticoids reduce mortality and the incidence of IVH in infants born at 24 to 28 weeks gestation.

Dexamethasone and Betamethasone have both been established to provide the above benefits. Dexamethasone has been associated with a higher incidence of neurologic complications.

The Society of Obstetricians and Gynaecologists of Canada (SOGC) and The American College of Obstetricians and Gynecologists (ACOG) supports the recommendations of the NIH Consensus Panel:

- The benefits of antenatal administration of glucocorticoids to fetuses at risk of preterm delivery vastly outweigh the potential risks. These benefits include a reduction in the risk of RDS, mortality and IVH.
- All women between 24 and 34 weeks of pregnancy at risk for preterm delivery are candidates for antenatal glucocorticoid therapy
- Fetal race, gender and availability of surfactant therapy should not influence the decision to use antenatal glucocorticoid therapy.
- Women eligible for therapy with tocolytic agents should be eligible for antenatal glucocorticoids
- Treatment should consist of two doses of betamethasone 12 mg intramuscularly (IM) given 24 hours apart.
- Optimal benefits begin 24 hours after initiation
- Treatment for <24 hours is still associated with significant reductions in neonatal mortality
- In women with complicated pregnancies for whom delivery prior to 34 weeks is likely, antenatal glucocorticoid use is recommended

BENEFITS

The greatest benefit is a substantial reduction in RDS. A single course of antenatal corticosteroids (ACS) reduces the risk of RDS from 46 to 20 percent in neonates born prior to 32 weeks. Reduction in IVH and neonatal mortality, less need for surfactant therapy, improved circulatory stability, and reduced requirement for oxygen and ventilation support.
**Risks**

ACS appears to have few adverse effects. There is no evidence of increased infection rates in infants, including cases with prelabour PROM. No clinically important adrenal suppression has been shown with a single course of ACS. There does not appear to be an increased risk of neurodevelopmental impairment as reflected in a greater prevalence of learning, behavioral, motor or sensory disturbances. A 12-year follow-up study indicated no significant differences between growth, lung, neurological or ophthalmological function in children who received ACS when compared to those who did not.

Potential adverse maternal effects include:

- Infection
- Accentuated glucose intolerance/hyperglycemia
- Pulmonary edema

**Protocols**

ACS is recommended for women 24 to 34 weeks gestational age

**Dosage**

Betamethasone 12mg IM 2 doses 24 hours apart

**Precautions**

- Avoid glucose screens within 48 hours
- When given to diabetic women, the diabetic regimen may need to be amended
- Will elevate WBC

In August of 2000, the National Institutes of Health (NIH) in the United States recommended against repeat courses of glucocorticoids. The 1994 recommendations still hold, but reworded. “All pregnant women between 24 and 34 weeks gestation who are at risk of preterm delivery within 7 days should be considered candidates for antenatal treatment with a single course of glucocorticoids.”

The “Multiple Courses of Antenatal Glucocorticoids for Preterm Birth Study” (MACS), a multi-centre, double-blinded randomized controlled trial, is currently ongoing to determine the effectiveness of multiple courses of ACS for women who continue to be at increased risk of preterm birth for seven or more days. The results of this trial are not available at this time.

**References:**

