South Australian Perinatal Practice Guidelines

# Preterm labour management



## Definition

- Preterm means a gestational age of less than $37^{+0}$ completed weeks of gestation (less than 259 days; FIGO 2009; Beck et al. 2010)

## Diagnosis

- Uterine contractions – may be difficult to differentiate from uterine irritability – frequency and especially regularity may be more meaningful than pain perception
- Shortening and dilatation of the cervix – reliable estimation essentially requires at least two observations separated in time
- Observational studies and placebo-controlled trials indicate that more than 50 % of women who present in preterm labour will continue their pregnancy (Kragt & Keirse 1990)

## Initial assessment

- History and examination
- Abdominal palpation to determine fetal size and presentation
- Speculum examination to:
  - Exclude PPROM
  - Visualise pooling of liquor (note presence of vernix)
  - Collect cervical and vaginal microbiological swabs (including GBS)
  - Make a smear to look for ferning on microscopical examination
  - Estimate cervical dilatation

### Transfer or retrieval for access to specialised obstetric and neonatal services

- In units without neonatal facilities suitable for the gestation, consult with tertiary centre. Consider maternal transfer if delivery is not imminent or consult with neonatal retrieval service if delivery is anticipated (for further information, refer to the PPG 'perinatal advice and emergency transport')

### Surveillance / fetal assessment

- Assess fetal wellbeing:
  - Cardiotocography (CTG) to assess fetal condition - interpretation should take early gestational age into account
  - Ultrasound examination for fetal number, size, presentation, fetal malformations (if morphology unknown), liquor volume and placenta localisation
  - Consider assessment of cervical length and dilatation (by vaginal scan) and umbilical artery flow

### Laboratory investigations

- C-Reactive Protein – repeat daily for three days
- Complete blood picture – repeat daily for three days
- Low and high vaginal swabs for microscopy and culture
- Midstream specimen of urine for bacteriology

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## Management

- Inform neonatologists of admission so they can arrange to meet and counsel parents if necessary
- Outcomes for preterm infants depend on place of birth and access to neonatal intensive care. Maternal transfer is generally safer than neonatal retrieval if delivery is not imminent

## Antibiotic prophylaxis and treatment

### Controlled trials

- Show a reduction in maternal infection with the use of antibiotics (prophylactically) for preterm labour with intact membranes but show no benefit in neonatal outcomes (King, Flenady 2002)
- Show that antibiotic treatment for bacterial vaginosis does not reduce the risk of preterm birth before $37^{+0}$ weeks or the risk of preterm prelabour rupture of the membranes (McDonald et al. 2007)

### No evidence of chorioamnionitis

- Consider tocolysis dependent on gestational age
- If labour is not arrested, give IV benzylpenicillin 3g loading dose, then 1.2 g IV every 4 hours for 48 hours or until delivery if this occurs before 48 hours, (unless GBS status is documented to be negative at presentation)

### Signs of chorioamnionitis:

Diagnosis of chorioamnionitis relies on the clinical presentation

- Maternal fever > 38° C with any 2 of the following:
  - Increased white cell count (> 15 x $10^9$/L)
  - Maternal tachycardia (> 100 bpm)
  - Fetal tachycardia (>160 bpm)
  - Uterine tenderness
  - Offensive smelling vaginal discharge
  - C-Reactive Protein > 40
- Histological examination of placenta and membranes with evidence of acute inflammation may confirm diagnosis after birth

### If signs of chorioamnionitis

- Ampicillin (or amoxycillin) 2 g IV initial dose, then 1g IV every 4 hours,
- Gentamicin 5 mg / kg IV daily
- Metronidazole 500 mg IV every 12 hours
- If allergic to penicillin, give lincomycin 600 mg IV in 100 mL over 1 hour every 8 hours or clindamycin 450 mg IV in 50 – 100 mL over at least 20 minutes until delivery
- Do not inhibit labour, but consider hastening delivery under intravenous antibiotic cover
- Consider optimal mode of delivery (LSCS versus vaginal birth) on the basis of the findings and the anticipated duration until birth

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### Postnatal maternal antibiotics

- If chorioamnionitis, consider treatment with continued:
  - Ampicillin (or amoxycillin) 1g IV every 4 hours
  - Gentamicin IV 5 mg / kg as a single daily dose
  - Metronidazole 500 mg IV every 12 hours for 5 days
- May change to oral antibiotics once the woman is afebrile and tolerating oral medication e.g. amoxycillin 500 mg every 8 hours and metronidazole 400 mg every 12 hours or amoxycillin / clavulanic acid (Augmentin Duo Forte x 1 every 12 hours) for the rest of the 5 days

## Tocolytics

### Controlled trials

- Show that tocolytic drugs may delay birth and reduce the occurrence of preterm birth
- Have thus far failed to show effects of betamimetics, magnesium sulphate or atosiban on significant adverse perinatal outcomes, such as respiratory distress and perinatal mortality
- The use of calcium channel blockers is associated with fewer side effects, but a systematic review on the subject (King et al. 2003) provides more questions than answers on its effectiveness and perinatal outcome

## Calcium channel blockers – nifedipine

- Advantages over betamimetics (in the comparative studies):
  - Oral administration
  - Possibly higher efficacy
  - Fewer side effects
- Indicated for suppression of preterm labour at less than $34^{+0}$ weeks

### Dosage

- Refer to the PPF 'Nifedipine use in preterm labour'

## Betamimetics (salbutamol)

- Salbutamol is the betamimetic used in Australia
- Salbutamol has never been compared with either placebo or no treatment in preterm labour; all evidence in favour of its use is derived from analogy with other betamimetic agents
- Available evidence does not support the use of oral betamimetics for maintenance after threatened preterm labour
- Intravenous betamimetic treatment may cause pulmonary oedema (especially when associated with fluid overload) and has been responsible for maternal deaths

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## Indications

- Given as IV salbutamol infusion (see below)
- Suppression of preterm labour at less than $34^{+0}$ weeks
- May be used as tocolytic cover for in-utero transfer of a woman in threatened preterm labour to a level IV or V hospital

## Contraindications

- Cardiac disease
- Hyperthyroidism
- Poorly controlled maternal diabetes mellitus
- Placental abruption or significant bleeding of unknown cause
- Chorioamnionitis
- Doses that create excessive maternal (140 bpm) or fetal (180 bpm) tachycardia should be avoided
- Relative contraindication in multiple pregnancy

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# Preterm labour management



## Salbutamol intravenous infusion regimens

- IV access
- Mainline of 1,000 mL hartmann's or 0.9 % sodium chloride
- Attach salbutamol infusion (with medication added label) using a three way tap to mainline (minimise dead space)
- Administer salbutamol either from the syringe or volumetric pump

| Syringe pump | Infusion pump |
|---|---|
| **Set up**<br>- Add 7.5 mg salbutamol (7.5 mL) to 42.5 mL sodium chloride 0.9 % OR 5 % glucose in syringe (50 mL total)<br>- Using medication added label write "salbutamol 150 micrograms per mL" and attach label to syringe | **Set up**<br>- Withdraw 15 mL from a 100 mL bag of sodium chloride 0.9 % or glucose 5 %<br>- Add 15 mg (15 mL) Salbutamol to the remaining 85 mL bag of sodium chloride 0.9 % or glucose 5 % (100 mL total)<br>- Using medication added label write "salbutamol 150 micrograms per mL" and attach label to bag |

### Dosage and administration

- Commence at 1 mL / hr = 2.5 micrograms per minute
- Increase rate at 10 minute intervals until response shown by decreased frequency, strength and length of contractions
- Increase rate slowly thereafter, until contractions cease
- Maintain infusion at same rate for 24 hours and then decrease at 1 mL / hr

**Decrease if:**

- Maternal pulse > 140 bpm
- Fetal heart rate > 180 bpm
- Hypotension
- Other side effects, e.g. dyspnoea, chest pain, palpitations, nausea and vomiting
- Women should also be warned about tremors, anxiety, dizziness and headaches
- Evaluate decreased contractions, maternal and fetal well-being
- The dose is determined by the woman's tolerance (i.e. clinical indicators) of adverse affects against desired response
- The dose should never exceed 45 micrograms / min (18 mL / hr)
- Betamimetics can cause a fall in serum potassium (K+). This is related to the movement of K+ intracellularly and is usually limited and self reversing. **No treatment is needed unless ECG changes occur** or the serum potassium falls below 2.5 mmol / L

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# Preterm labour management



## Inhibitors of prostaglandin synthesis (indomethacin)

- Inhibitors of prostaglandin synthesis (indomethacin in particular) are the most potent inhibitors of uterine contractility currently available. They inhibit the cyclo-oxygenase (COX) enzyme of which two varieties exist (Cox-1 and Cox-2). Inhibitors currently used inhibit both enzymes although more specific Cox-2 inhibitors have been developed
- Few adequate trials of prostaglandin synthesis inhibitors in preterm labour exist in the literature and information needs to be derived from other sources to obtain sufficiently valid guidelines on their use

### Indications

- Because of the potential adverse fetal and neonatal effects the use of indomethacin (the most commonly used cyclo-oxygenase inhibitor in preterm labour) should probably be restricted to:
  - Gestational ages of < $28^{+0}$ weeks
  - Failure to achieve tocolysis with other tocolytic regimens
  - Contraindications to other tocolytics (e.g. cardiac disease)
  - Administration for a short period of time (1 – 3 days)

### Contraindications and risks

- Risks for the fetus and neonate include:
  - Constriction of the fetal ductus arteriosus (the risk increases with advancing gestational age; the effects are transient and reversible with short term administration; longer administration may lead to pulmonary hypertension in the fetus and neonate)
  - Alteration of fetal (especially cerebral) blood flow
  - Reduced renal function (may result in oligohydramnios)

### Dosage

- Indomethacin has a short half-life and frequent administration of low doses is recommended instead of administering higher doses infrequently
- Start treatment with 100 mg or 50 mg (absorption after rectal and oral administrations are similar)
- Repeat after 4 hours (reduce to half of the starting dose if some uterine quiescence is achieved)
- Administer 25 mg (or 12.5 mg) every 4-hours, but for no longer than 48-72 hours
- ***With indomethacin administration, ensure close monitoring of fetal wellbeing***

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## Progesterone

- A systematic review (Romero et al. 2012) has shown convincing evidence that daily vaginal administration of progesterone reduces the risk of preterm birth in women with a short cervix demonstrated by ultrasound in mid-pregnancy. There might also be benefit in women with other significant risk factors for preterm birth (see risk factors in PPG 'cervical incompetence and cerclage')
- Doses of vaginal progesterone have been 90 mg in gel preparation and 200 mg in pessary form. A 200 mg pessary nocte to women who are shown to have a cervix < 20 mm at 19-$24^{+0}$ weeks gestation until 34 weeks gestation, prelabour rupture of the membranes or delivery can be recommended (Royal Hospital for Women 2008; 3centres Collaboration 2011; Romero et al. 2012)

## Corticosteroids

- Corticosteroids are effective in preventing adverse perinatal outcomes, most notably respiratory distress syndrome, and in increasing the likelihood of neonatal survival (Roberts, Dalziel 2008)
- Repeated doses of corticosteroids reduce the occurrence and severity of neonatal lung disease and the risk of serious health problems in the first few weeks of life

### Dosage

- Administer IM betamethasone in two doses of 11.4 mg (5.7 mg x 2) 24 hours apart to the woman if birth is likely to occur between $23^{+0}$ and $35^{+0}$ weeks
- If betamethasone is unavailable, give IM dexamethasone in two doses of 12 mg, 24 hours apart (Elimian et al. 2007)

### Repeat doses

- Administer IM betamethasone 11.4 mg (5.7 mg x 2) one week after the initial dose
- Continue weekly dose IM betamethasone 11.4 mg (5.7 mg x 2) until delivery or $32^{+0}$ weeks of gestation
- If betamethasone is unavailable, give weekly dose of IM dexamethasone 12 mg until delivery or $32^{+0}$ weeks of gestation

## Magnesium sulphate for neuroprotection of the fetus

### Controlled trials

- Show that fetal exposure to magnesium sulphate given before preterm birth has a neuroprotective role. The number of women needed to be treated to benefit one baby by avoiding cerebral palsy is 63 (Doyle et al. 2009)
- This systematic review also showed a significant reduction in the rate of gross motor dysfunction in early childhood (Doyle et al. 2009)

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### Indications

- Neuroprotection of the fetus for women at risk of preterm birth who are at least $24^{+0}$ weeks of gestation and < $30^{+0}$ weeks of gestation
- When birth is anticipated within 24 hours or in cases of expected planned delivery as close to four hours before expected delivery time and regardless of;
    - plurality
    - why the woman is at risk of preterm birth
    - parity
    - anticipated mode of birth
    - whether antenatal corticosteroids have been given or not

### Dosage and administration

- Refer to the PPG 'Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus'

## Mode of delivery

- The available trials of caesarean section versus vaginal birth to determine the best route of delivery are too small to draw clinical conclusions from them (Grant and Glazener 2003)
- The following general suggestions are reasonably well supported by clinicians:

### Less than $26^{+0}$ weeks

- Cephalic presentation - Vaginal birth
- Breech presentation – If aggressive neonatal management anticipated then caesarean section may be the safest mode of delivery if time permits. If the baby is at borderline viability and for example in a non-tertiary setting then vaginal birth may be more appropriate
- Multiple pregnancy – Caesarean section
- Consider the use of uterine relaxation techniques (e.g. glycerol trinitrate) for difficult delivery of the head (either vaginal birth or caesarean section)
    - The recommended dose of glycerine trinitrate is 50-100 micrograms IV or one metred dose of sublingual spray ( 400 micrograms)

### $26^{+0}$ weeks or greater

- Cephalic presentation - vaginal birth
- Breech presentation - caesarean section

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## Care of the newborn infant

### Place of delivery

- Singleton pregnancy ≤ 33 weeks, Multiple pregnancy ≤ 34 weeks - birth in a hospital with neonatal intensive care (Level VI) facilities
- Singleton pregnancy ≥ 33 weeks, Multiple pregnancy ≥ 34 weeks - birth in a hospital with at least level V (or level VI) facilities
- ≥ 35 weeks – birth in a hospital with at least level IV facilities
- ≥ 37 weeks – birth in a hospital with at least level III facilities

### Care at delivery

- Attendance of a paediatrician / neonatologist / neonatal nurse practitioner at the time of birth is essential
- May also require assistance from a neonatology nurse
- Postnatal (neonatal) care is the responsibility of the neonatologist (taking the maternal history and the condition of the infant at birth into account)

## Cord blood and placenta

- Cord blood samples (arterial and venous) should be collected for blood gas analysis
- Collect and send placenta for:
  - Histopathology (including check for chorioamnionitis)
  - Swabbing for microbiological evidence of infection

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## Abbreviations

| | |
|---|---|
| bpm | Beats per minute |
| C | Celsius |
| CBP | Complete blood picture |
| CRP | C-reactive protein |
| COX | cyclo-oxygenase enzyme |
| ° C | Degrees Celsius |
| CTG | Cardiotocography |
| et al. | And others |
| e.g. | For example |
| FIGO | International Federation of Gynecology and Obstetrics |
| g | Gram(s) |
| GBS | Group B Streptococcus |
| IM | Intramuscular |
| IV | Intravenous |
| kg | Kilogram/s |
| mL | Millilitre/s |
| mg | Milligram/s |
| WHO | World Health Organisation |

## Version control and change history

**PDS reference:** OCE use only

| Version | Date from | Date to | Amendment |
|---|---|---|---|
| 1.0 | 10 May 04 | 29 Dec 08 | Original version |
| 2.0 | 29 Dec 08 | 21 May 11 | Reviewed |
| 3.0 | 21 May 11 | 22 May 12 | Reviewed |
| 4.0 | 22 May 12 | current | |

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