Pre-term birth (intact membranes)

Target audience	Healthcare professionals caring for women at increased risk of, with symptoms and signs of, pre-term birth (PTB), or women having planned PTB. Commissioners and providers of maternity care services.
Patient group	Women with a singleton pregnancy at increased risk of, or with symptoms and signs of, PTB (before 37 weeks of gestation), and women with a singleton pregnancy having a planned PTB. It aims to reduce the risks of PTB for the baby and describes treatments to prevent or delay early labour and birth.

Related documents

This guideline covers PTB with intact membranes only. Please also see the following related guidelines available on the Right Decisions app and on FirstPort:

- Guideline for Preterm Prelabour Rupture of Membranes at Term - Preterm Prelabour Rupture of Membranes
- Guideline for the Management of GBS Intrapartum Antibiotic Prophylaxis - gbs-intrapartum-antibiotic-prophylaxis-v2-may-2021-281021.pdf
- Guideline for Fetal Heart Rate Monitoring in Labour - fetal-heart-rate-monitoring-in-labour-v2-june-2021-281021.pdf
- Guidelines related to the Birth of an Extremely Premature Infant (22+0 – 22+6 weeks gestation) - guidelines-relating-to-the-birth-of-an-extremely-premature-infant-22plus0-26plus6-weeks-gestation.pdf
- Corticosteroids Administration in the Antenatal Period to Reduce Neonatal Morbidity - corticosteroids-administration-in-the-antenatal-period-to-reduce-neonatal-morbidity.pdf
- Antanatal Magnesium Sulphate for Neuroprotection of the Preterm Infant - antenatal-magnesium-sulphate-for-neuroprotection-of-the-preterm-infant-july-2022.pdf
- Standard Operating Procedure: Actim Partus and Actim - Home - Point of Care Testing

Summary

- Ensure verbal and written patient information and support is provided as early as possible.
- Describe symptoms and signs of preterm labour.
- Initial assessment should include a detailed history, observations, examination and investigations (including an portable ultrasound scan for presentation).

- Actim Partus is a reliable point-of-care test which can be used to identify pregnant women with a risk of PTB.
- Transvaginal assessment of the cervix can be more useful in assessing the risk of PTB compared with a speculum examination.
- Tocolysis should only be offered in a select cohort of women, where delaying birth could be of short-term benefit, for example to give steroids and/or transport the woman to an alternative birthing location. Consider nifedipine as first-line.
- Offer maternal corticosteroids between 24+0 and 33+6 weeks of gestation.
- Magnesium sulphate ($MgSO_4$) should be offered to all women with suspected or anticipated PTB between 24+0 and 29+6 weeks of gestation.
- Antibiotics should be administered in confirmed PTB (according to local NHSL guidance) and should provide cover for group B streptococcus (GBS).
- Do not use fetal scalp electrode (FSE) for monitoring the fetal heart at less than 34+0 weeks of gestation.
- Do not perform fetal blood sampling (FBS) at less than 34+0 weeks of gestation.
- Mode of delivery should be discussed with and decided upon in conjunction with the woman with informed discussion around risk and benefits. Consider caesarean birth if the fetus is in the non-cephalic position.
- Offer delayed cord clamping (DCC) where appropriate (at least 60 seconds).
- Offer delivery into plastic bags for all babies less than 32+0 weeks of gestation.
- Encourage breast feeding as part of the early breast feeding initiative.

Contents

Background

Pre-term labour (PTL) is defined as uterine contractions with cervical effacement and dilatation prior to 37+0 weeks of gestation. Pre-term birth (PTB) is when delivery of the fetus occur as a result of this. There are multiple gestation-specific terms used to describe the spectrum of PTB:

- **Pre-term birth (PTB)** is the general term describing the birth of a baby at less than 37+0 weeks of gestation.
- **Extreme PTB** is where birth occurs before 28+0 weeks of gestation.
- **Early PTB** is where birth occurs between 32+0 and 33+6 weeks of gestation
- **Late PTB** is where birth occurs between 34+0 and 35+6 weeks of gestation.

Premature infants are at greater risk of cerebral palsy, developmental delay, hearing problems and problems with their vision. The earlier a baby is born, the greater the risk. Brain injury ("encephalopathy of prematurity") is common among pre-term babies, ranging from white matter injury to intraventricular and cerebellar haemorrhages.

PTB is the commonest cause of death among infants worldwide. About 15 million babies are born pre-term each year (5-18% of all deliveries). The UK average for PTB sits at around 7.9%. The chance of survival is as follows:

- 6% at 22 weeks of gestation
- 26% at 23 weeks of gestation
- 55% at 24 weeks of gestation
- 72% at 25 weeks of gestation

In general, we are most concerned with PTB occurring between 22+0 and 32+6 weeks of gestation:

- At less than 22+0 weeks of gestation, the outlook for the infant is poor and we do not usually provide medical intervention to prevent established PTB.
- After 34+0 weeks of gestation, the outlook for the infant is good and we do not usually provide medical intervention to prevent established PTB.

Information and support

- Support and information should be given to the woman and her family as early as possible as PTB can progress very quickly. Patients who are identified as high-risk for PTB should be informed in a timely fashion of the symptoms and signs to be aware of and where and when to seek help if needed. This should be done both verbally and in written format.

- Each woman is different but all will need multidisciplinary care from senior staff.
- It is important to involve the neonatal team as soon as possible. Ensure the patient is aware of the likely neonatal journey. Information leaflets can be useful for this purpose. This makes understanding easier.
- As per NICE guidelines, women and their families should be involved in discussing the following:
    1. Survival rates.
    2. Expected neonatal care.
    3. Short- and long-term consequences.
    4. Parental wishes for resuscitation.
    5. Potential for a tour of the neonatal unit in University Hospital Wishaw (UHW).
- The neonatal team forms an integral part of the multidisciplinary team (MDT) and should be consulted both antenatally and at birth e.g. optimal cord clamping (see relevant local guideline).
- The British Association of Perinatal Medicine (BAPM) is a good resource for getting up-to-date advice on the management of pre-term babies.

Perinatal wellbeing package

See appendices 1 and 2. These are approved interventions by the National Neonatal Audit Programme (NNAP). They have seven points of interventions, proven to improve neonatal outcomes. These measures have been shown to reduce mortality and morbidity such as intraventricular haemorrhage (IVH), sepsis, necrotising enterocolitis (NEC) and cerebral palsy (CP).

Initial assessment

This should include:

- reviewing case notes on BadgerNet
- risk assessment
- History:
    - Contractions - duration, strength, frequency
    - Pain – location, frequency, severity
    - Vaginal loss (discharge, show, liquor ('gush of fluid') and/or bleeding)
    - Altered or reduced fetal movements (RFM)

- Urinary symptoms

- Observations (document on the MEOWS chart) including pulse, blood pressure, temperature, respiratory rate and oxygen saturations
- Urinalysis +/- mid-stream specimen of urine (MSSU)
- Abdominal examination: fundal height, lie, presentation, palpate contractions
- Speculum examination +/- vaginal swab if indicated
- Actim Partus (if appropriate)
- Vaginal examination (if indicated to assess cervical dilatation)
- Bloods – full blood count, C-reactive protein and group and save
- Bedside ultrasound for presentation

Established labour is defined as cervical dilatation of 2cm or more. In-utero transfer (if required) is not recommended at more than 4cm cervical dilatation.

Point-of-care testing to assist in the diagnosis of PTB

- **Actim Partus** tests for insulin-like growth factor binding protein-1 (IGFBP-1) in cervical secretions. IGFBP-1 is made by cells lining the uterus. When delivery is imminent, small amounts leak into the cervix.
- This is a small cassette which is read in a similar fashion to a home pregnanct test. The presence of two lines indicates a high chance of labour in the next 7-14 days. This should **not** be used after bleeding.
- **Please note that Fetal fibronectin (FFN) is no longer available in the UK due to supplier issues. It has been kept in the guideline in case supplies resume.**
- **FFN** is an adhesive glycoprotein that helps to keep the amniotic sac attached to the uterine lining. After 35 weeks of gestation, they naturally begin to breakdown. If detected in vaginal secretions between 22+0 and 33+6 weeks of gestation, it is an indicator of PTB.
- A negative result means a woman is unlikely to labour and can usually go home with worsening advise. Always think of other diagnoses.
- A positive result (50ng/ml or more) means PTB is likely, and steroids and tocolysis should be considered.
- Test results can be invalidated by the presence of semen, cervical dilatation, intercourse and blood, but a negative result should still be considered reassuring.

Tocolysis

Tocolysis may be useful in a select group of women where delay for the purpose of steroid administration or transfer to an alternative birth location is indicated. When making a decision to administer tocolysis, consider the following contraindications:

- Lethal congenital abnormalities
- Chromosomal anomalies
- Intrauterine infection (chorioamnionitis)
- Severe pre-eclampsia/eclampsia
- Antepartum haemorrhage
- Placental abruption
- Advanced cervical dilatation (>4cm)
- Evidence of fetal compromise or placental insufficiency

- Consider tocolysis between 24+0 and 25+6 weeks of gestation, as some benefit may be gained from prolonging pregnancy. (e.g. improving fetal weight, where resuscitation can be more effective).
- Offer tocolysis between 26+0 and 33+6 weeks of gestation.
- Tocolysis **should not** be offered in women with ruptured membranes.
- Nifedipine is the first-line medication.
- This is a calcium-channel blocking agent that can inhibit contractions.
- Alternatives to nifedipine include atosiban and indomethacin.
- Before considering combinations of tocolytic drugs, the obstetric consultant should be notified.
- In idiopathic PTL a combination of drugs should be used if one tocolytic drug is not sufficient to inhibit PTL at its maximum doses.
- Suitable combinations:
    - Atosiban and indomethacin – only if less than 32+0 weeks of gestation
    - Atosiban and nifedipine – do not given if maternal hypotension
- For dosages and alternatives, please refer to appendix 3.

Maternal corticosteroids

Glucocorticosteroids are anti-inflammatory medicines given to the women (usually by an intramuscular injection), which cross the placenta and accelerate fetal lung maturity. Giving corticosteroids to a woman before PTB reduces the severity of lung disease of prematurity and also potentially reduces the length of neonatal intensive care unit (NICU) stay and ventilatory requirements. Extreme premature babies require an individualised approach made in liaison with the neonatal Team.

Gestation-specific recommendations:

- Consider corticosteroids between 22+0 and 23+6 weeks of gestation.
- Offer corticosteroids between 24+0 and 33+6 weeks of gestation.
- Consider corticosteroids between 34+0 and 35+6 weeks of gestation (eg severe fetal growth restriction).

Repeated corticosteroid administration is rare but can be considered when the first course was more than 7 days ago, and it is felt that the woman is likely to birth within the following 48 hours. Repeated doses have been linked with fetal growth restriction so should be reserved for specific women with documented agreement from the obstetric consultant. NICE currently recommends that no more than two courses should be administered.

Steroids can increase blood sugar levels so extra care is needed in diabetic women, especially those with poor control or who are insulin-controlled. Please refer to "Managament of Diabetes and Delivery" guideline on the RDS app for further information.

Steroids can also cause neonatal hypoglycaemia and hyperinsulinemia. Even transient and treated neonatal hypoglycaemia can be associated with adverse childhood outcomes. The Dutch Longitudinal Preterm Outcome Project (LOLLIPOP) of moderate preterm children (born at 32^{+0} to 35^{+6} weeks) suggested links with hypoglycaemia, respiratory morbidity and developmental delay at four years of age.

There is little data regarding risks and benefits of antenatal corticosteroids in multiple pregnancies and other high-risk obstetric groups (Roberts et al 2017).

For dosages please refer to appendix 3.

Magnesium sulphate ($MgSO_4$)

Gestation-specific recommendations:

- Consider magnesium sulphate between 22+0 and 23+6 weeks of gestation.
- Offer magnesium sulphate between 24+0 and 29+6 weeks of gestation, even in planned PTB.
- Consider magnesium sulphate between 30+0 and 33+6 weeks of gestation.

Monitor for signs of magnesium toxicity every 4 hours:

- maternal pulse (looking for bradycardia)
- blood pressure
- respiratory rate.
- deep tendon reflexes (e.g. patellar).
- Oliguria
- Somnolence
- Respiratory depression
- Respiratory/cardiac arrest

If there are concerns regarding possible magnesium toxicity:

- Stop the infusion immediately
- Increase frequency of monitoring as above
- Send serum magnesium levels

- Consider administration of 10ml 10% calcium gluconate over 10 minutes
- Involve senior anaesthetic and obstetric staff

For dosages, please refer to appendix 3.

Repeated doses of intravenous magnesium sulphate is not usually repeated for the purposes of neuroprotection of the infant but note that repeated doses can be given in cases of severe pre-eclampsia/eclampsia.

Antibiotics

- Intrapartum antibiotics should be offered to all women labouring prior to 37+0 weeks of gestation.
- This is to minimise the risk of GBS transmission to the infant.
- Exercise caution with administration of coamoxiclav as this has been associated with an increased risk of NEC.

Fetal monitoring

- A normal cardiotocograph (CTG) is reassuring and indicates a non-compromised fetus. However, an abnormal trace does not necessarily indicate fetal hypoxia or acidosis.
- When established in pre-term labour, CEFM is recommended.
- FSE's should not be used before 34+0 weeks of gestation unless there is no alternative to provision of CEFM. This should be done only with agreement from the consultant obstetrician.
- FBS should not be carried out before 34+0 weeks of gestation.
- Between 34+0 and 35+6 weeks of gestation, the use of FSE and FBS should be carefully discusse with the woman given the increased risk of infection, bleeding and fetal trauma.

Mode of birth

- This is highly individualised decision based on factors specific to each woman.
- Both caesarean and vaginal birth can be offered.
- Caesarean birth can be complicated by use of midline laparotomy and vertical uterine incisions, both of which may increase morbidity and have a negative impact on future obstetric health.
- Caesarean birth is not any safer or riskier for the baby compared with vaginal birth.
- Consider caesarean birth between 26+0 and 36+6 weeks of gestation for breech presentation.

- Ventouse and Kiwi omnicup delivery should not be attempted prior to 34 weeks of gestation.

Optimal cord clamping

- Clamping of the fetal umbilical cord should be delayed by at least 60 seconds.
- This shoud be done at both caesarean and vaginal births.
- The baby should usually be positioned at or below the level of the placenta before clamping. However, this needs to be tailored according to the individual patient and case. This should be discussed with the neonatal team to allow consideration of temperature control, maintaining a neutral airway and ability to perform this if the use of a plastic bag is warranted.
- There are very few contraindications but these are listed below:
    - Massive maternal haemorrhage with the need for acute resuscitation.
    - Cord issues such as ruptured vasa praevia, snapped cord or lack of cord integrity, all of which could lead to significant fetal haemorrhage.
    - Fetal death.
    - Twin-to-twin transfusion syndrome (TTTS).

Plastic bags

Consider delivery into plastic bags for all preterm, and small for gestational age (SGA) babies, to prevent neonatal hypothermia. A recent Cochrane review of interventions to prevent hypothermia in preterm neonates suggested that plastic bags reduced heat losses by 0.7 °C in neonates <28 weeks, with a 44% reduction in observed hypothermia.

Breast-feeding

- All pregnant women, including those expected to deliver pre-term, should have a discussion with midwifery and medical staff around benefits of early breast-feeding for the baby, including reducing the risks of infection, diarrhoea, vomiting, sudden infant death syndrome (SIDS) and obesity.
- There should be focus on maternal expressed breast milk (MEBM) in the first 24 hours of life and mothers should be supported to express as soon as possible after birth.
- Early nutrition plays an important role in achieving optimised short and longer term health, and the aims of nutritional management are to:

1. Achieve an adequate standard of short and longer term growth
2. Meet the increased nutritional requirements of the preterm baby
3. Avoid feeding-related morbidities, especially NEC
4. Optimise longer term health outcomes such as neurodevelopmental attainment

- A consistent approach to enteral feeding is advocated because data from multiple observational studies suggest that the use of a standardised feeding guideline positively impacts a number of clinical outcomes including:
    - Reduced time taken to achieve full milk feeding
    - Shortened time on the postanatl wards
    - Shortened length of hospital stay
    - Reduced NEC rates
    - Improved growth and neurodevelopmental attainment.

Special considerations

Cervical length (CL) scanning

NICE guidelines suggest using transvaginal ultrasound to measure cervical length to check for pre-term labour in women less than 30+0 weeks of gestation:

- If CL is less than 15mm, pre-term labour is confirmed.
- If CL is more than 15mm, pre-term labour is unlikely - think of alternate diagnoses for presenting symptoms, and consider discharge with worsening advice.

Transvaginal ultrasound should only be performed by experienced healthcare professionals with the appropriate training.

Cervical cerclage

This is rarely justified beyond 24+0 weeks of gestation. It is contraindicated in suspected or confirmed infection, vaginal bleeding, fetal compromise, lethal fetal anomaly and intrauterine death/stillbirth. Emergency cerclage can be offered to women in pre-term labour, where membranes are intact and not bulging and if the cervix is less than 4cm dilated. It can prolong pregnancy by 34 days on average, with limited data on improved neonatal outcomes. Further details on cervical cerclage is outwith the scope of this guideline.

Vaginal swabs

Vaginal swabs are not routinely indicated, unless there is evidence or suspicion of infection.

References

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Appendix 1 – care pathway for preterm optimization

Correct place for birth

Appropriate neonatal support available, inform neonatal unit on call of admission as soon as possible

Magnesium sulphate

Consider between 22+0 and 23+6
Offer between 24+0 and 29+6
Consider between 30+0 and 33+6
Complete 24 hours if possible

Intrapartum antibiotics

All women in established labour before 37 weeks of gestation as GBS prophylaxis

Steroids

Consider between 22+0 – 23+6
Offer between 24+0 – 33+6
Consider between 34+0 – 35+6

Delayed cord clamping

All babies (unless contraindicated) for at least 60 seconds

Temperature regulation and breast feeding

According to Lanarkshire neonatal policy

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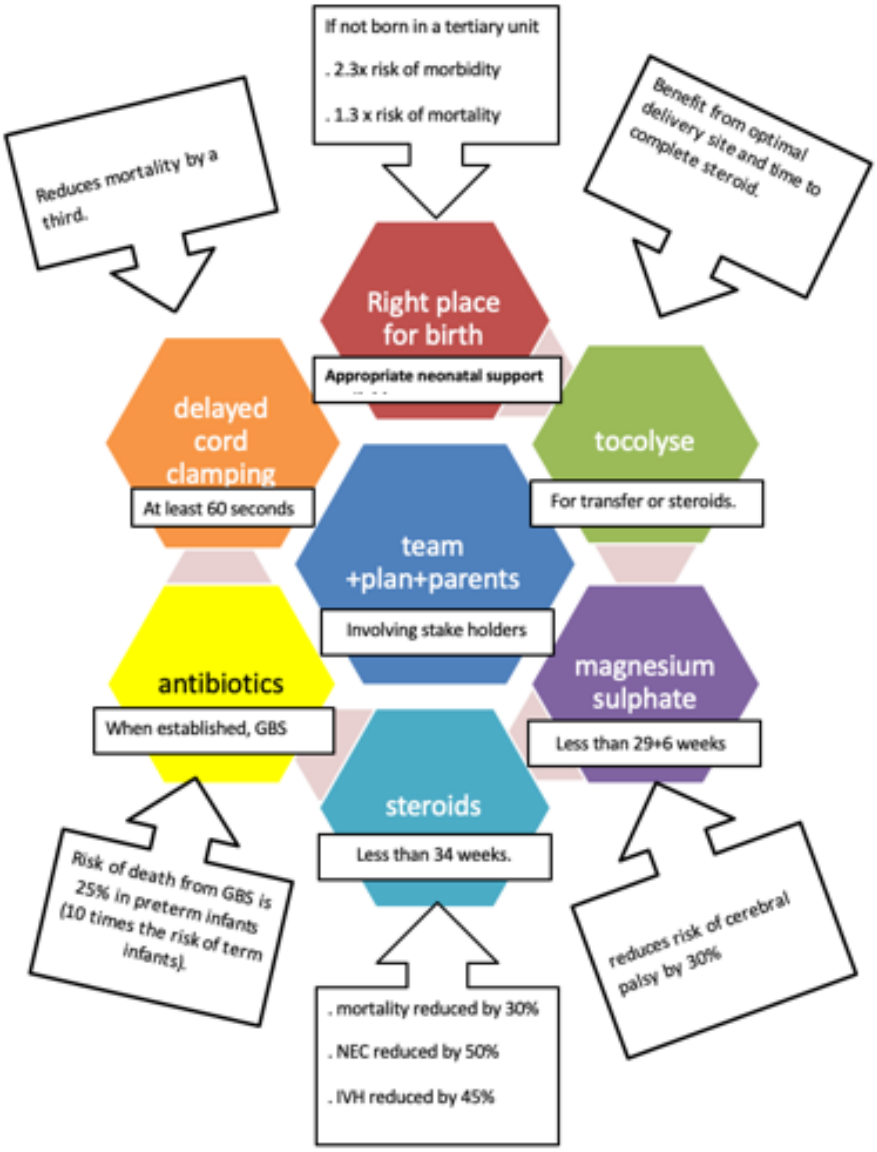
Appendix 2 – infographic for pre-term perinatal wellbeing package



Appendix 3 – medications

Medication	Dosages	Caution/ side effects	Contraindication
Nifedipine (calcium channel blocker)	20 mg oral 3-4 times/day adjusted to UA. Don't use slow release or sublingual	Maternal hypotension (BP less than 100 mg/Hg systolic).	See main text Porphyria Cardiac disease
Atosiban (oxytocin receptor antagonist)	Loading dose- 6.75 mg IV over 1 minute Maintenance dose- Add 2x 5ml ampoules (7.5 mg/mL) to 90ml normal saline = 0.75 mg/mL. 300 micrograms per minute for 3 hours, then reduce to 100 micrograms per minute for 45 hours.	Nausea Vomiting Tachycardia Hypotension Headaches Dizziness Hot flushes Hyperglycaemia Injection site reaction Pruritus etc.	
Indomethacin (anti-prostaglandin)	100 mg PR, 12 hourly for 48 hours (max. 4 doses)	More than 32 weeks of gestation	Dyspepsia Asthma Allergies Renal disease
Magnesium sulphate (MgSO4)	Loading dose – 4 g IV over 15 minutes Maintenance dose- 1g per hour (continue until birth or complete 24 hours, whichever is sooner)		
Betamethasone	2x IM injections of 12 mg betamethasone, 24 hours apart.(12 hours apart if delivery imminent)	1. IDDM 2.Suspected chorio-amnionitis	Placental abruption Systemic infection (incl. TB)

Clinical governance

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