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PRETERM BIRTH GUIDELINE

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Summary
Details for assessing risk of preterm birth and managing preterm and threatened preterm birth. Includes details on liaison with the neonatal team and conversations around limits of viability *Specifically details around use of antenatal steroids and magnesium sulfate.*

Version tracking			
Version	**Date Ratified**	**Brief Summary of Changes**	**Author**
NA		New guidance from merging separate guidelines	-

CONTENTS

SECTION A: PRETERM CLINIC

Women identified as being at risk of preterm birth (PTB) by their community midwives at their booking appointment should be referred using the attached form.

Referral criteria:

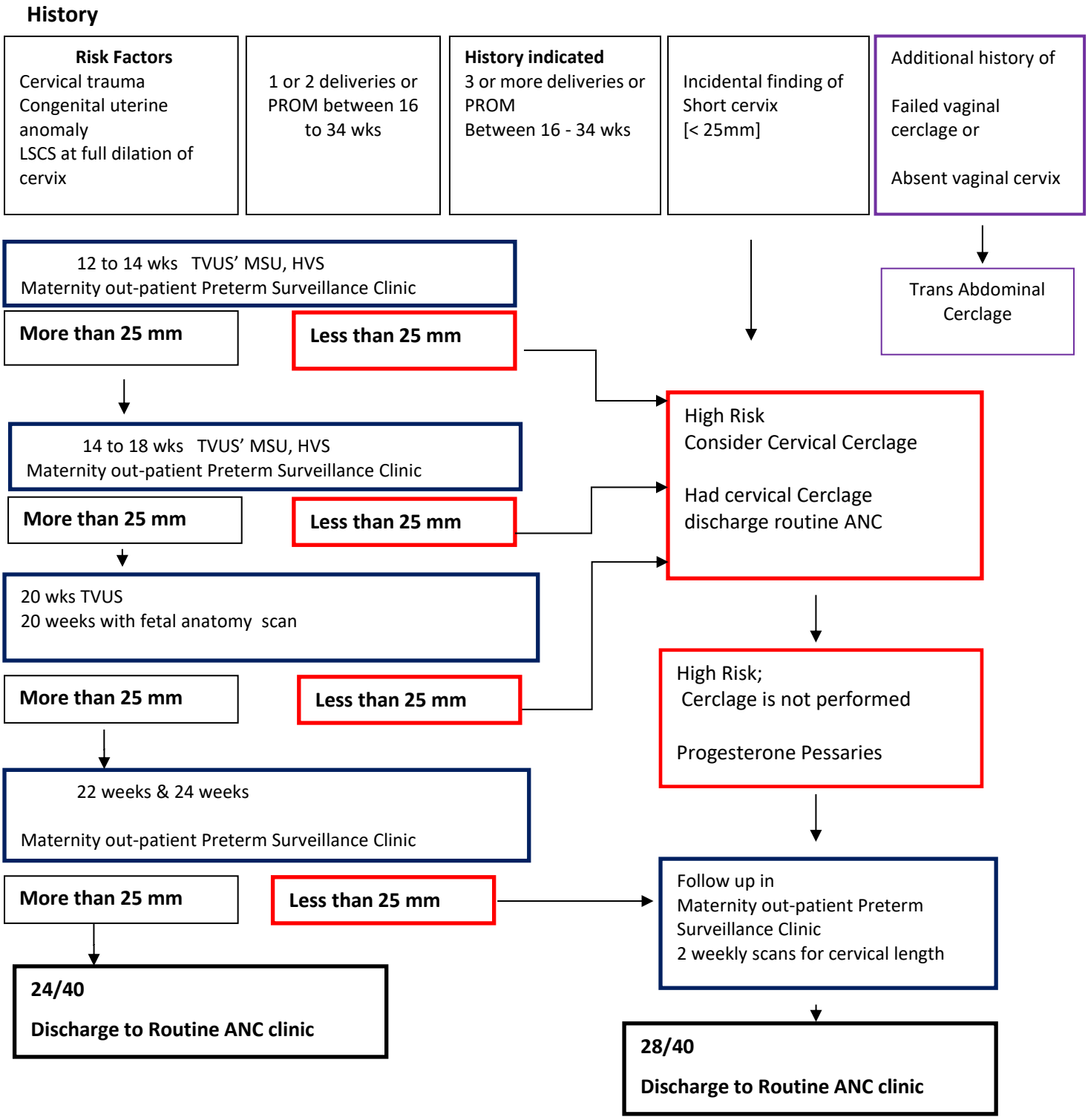
- High Risk:
  - Previous late miscarriage / preterm birth (16-34 weeks)
  - History of PPROM (16-34 weeks)
  - Previous second trimester losses
  - Congenital uterine anomalies – eg single uterine horn, hypoplastic uterus
  - Intrauterine adhesions
  - Trachelectomy
  - Cervical trauma – eg extensive tear of the cervix at previous delivery
  - History of cervical cerclage in previous pregnancies
- Intermediate risk:
  - Previous Caesarean section at full dilatation of the cervix
  - LLETZ:
    - Deep LLETZ – more than 1cm (can be determined from histology on ICE)
    - Two or more standard LLETZ

- For advice about referrals, please contact preterm-surveillance-clinic@porthosp.nhs.uk

During the Preterm Surveillance Clinic, patients will have 4-weekly HVS and MSU taken to screen for subclinical infection that can potentially lead to premature birth. They will have their blood pressure and urine dipped as per routine. An ultrasound machine will be available for transabdominal and transvaginal ultrasound.

Other responsibilities of the clinic include discussions with patients about lifestyle changes such as smoking / recreational drug cessation, and strategies to minimise stress, excessive working hours (including night shifts), and exposure to air pollution

Preterm Birth Algorithm for Prophylactic Interventions



For any clarification for cervical length scanning please contact the preterm Consultants

SECTION B: PRETERM LABOUR AND THREATENED PRETERM LABOUR

Where preterm labour cannot be prevented, there are a number of interventions which can improve the outcome for the neonate. Diagnosing and treating preterm labour therefore is of paramount importance.

Preterm labour is defined as regular uterine contractions, prior to 37 weeks of pregnancy, which result in changes of the cervix. These changes include effacement and dilatation.

Women often present to Maternity Assessment Unit (MAU) and labour ward (LW) with abdominal pain whilst preterm. Preterm labour must always be considered as a potential diagnosis. In earlier gestations (<28/40), sometimes a low backache or pressure is all that is reported. Any concern should prompt an abdominal and pelvic examination with speculum. Cardiotocograph (CTG) recordings can show tocographic activity of the uterus. This must be correlated with the woman's clinical symptoms. If preterm labour is diagnosed or suspected, antenatal corticosteroids, magnesium sulfate and tocolysis with nifedipine should be considered to allow time for the steroids. Please note that Nifedipine is contraindicated if there is thought to be bleeding from abruption.Use Magnesium sulfate with caution in patients presenting with bleeding, as it is also a week tocolytic.

Fetal Fibronectin

Fetal Fibronectin (fFN) is a glycoprotein found between the chorion and the decidua. It is often considered as the "glue" binding the fetal sac to the uterine lining.

The bedside test of fFN can provide strong negative predictive value that a patient's current clinical situation will not lead to immediate preterm delivery.

fFN Level	< 7 days (%)	< 14 days (%)	< 34 weeks (%)
<10 ng / ml	1%	1.8%	1.5%
10-49 ng/ml	0%	1.6%	8.2%
50-199 ng/ml	0%	7.7%	11.5%
200-499 ng/ml	14%	29%	33%
>500 ng/ml	38%	46%	75%

fFN should only be performed if the clinician is unsure of the diagnosis, or if it will change their management. Patients presenting with strong, regular palpable contractions who require gas and air or similar analgesia, or who have obvious changes to the cervix should be treated as PTL and do not require fFN. If the fFN test is < 100ng/ml,, the patient does not require steroids or tocolysis. They can be admitted for analgesia, but should not be considered at risk of delivery.

Relative contraindications – *(test can still be performed but more likely to be a false positive)*

- Moderate or gross vaginal bleeding
- Sexual intercourse within last 24 hours
- Previous digital vaginal examination

Contraindications

- Spontaneous rupture of membranes (SROM)
- Cervix greater than (>)3cm dilated

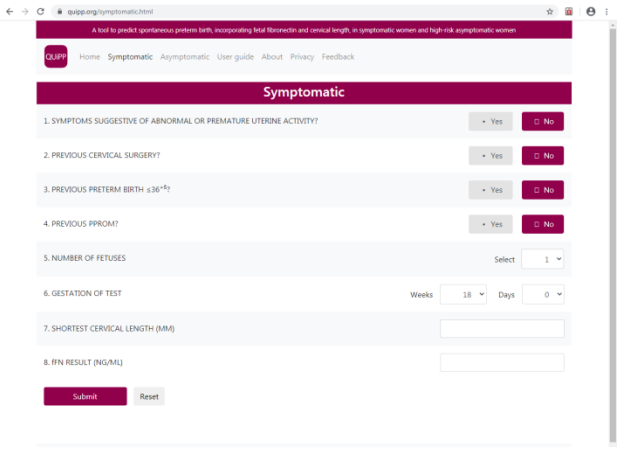
Concern has been raised over the use of lubricant gel used with speculum examination (Aquagel / KY Jelly) affecting the test. As-yet-unpublished data from the Preterm Surveillance Clinic at St Thomas's Hospital in London strongly shows that a small amount of lubrication will not affect the test result.

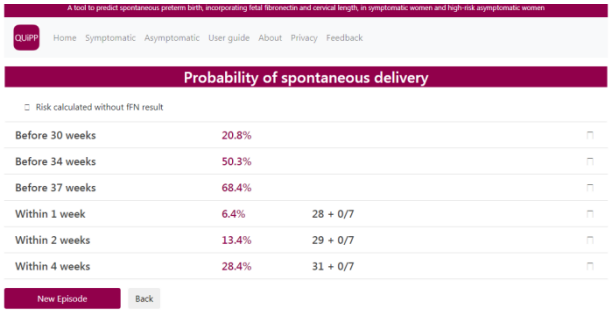
QUiPP: A tool to predict spontaneous preterm birth

The QUiPP app is a clinical decision-making tool for women with symptoms of threatened preterm labour as well as asymptomatic high-risk women. This application has been designed to calculate individualised % risks scores of delivery within pre-specified clinically relevant timeframes. It is designed to be used with women as an educational tool and to arrive at shared decisions regarding the management of their pregnancy.

It is designed for use in two clinical settings:

1. For management of asymptomatic women at high-risk for preterm birth (delivery before 37 weeks' gestation) who are attending preterm surveillance clinics
2. For management of women with symptoms suggestive of abnormal or premature uterine activity (e.g. abdominal pain, contractions, tightenings).
3. It relies on a relevant clinical history having been taken regarding the woman's risk factors for preterm birth and her current symptoms. It relies on existing point-of-care testing: quantitative fetal fibronectin (fFN) sampling of the cervico-vaginal fluid and/or transvaginal ultrasound cervical length (CL) measurements.





There is no one threshold at which to offer or not offer treatment, and must be done on an individual case by case basis.

SECTION C: ANTENATAL CORTICOSTEROIDS

Indication: Women admitted between 22+5 and 33+6 weeks gestation in whom there is a significant risk of preterm birth **within the next 7 days**, either spontaneous or iatrogenic, including:

- Preterm labour i.e. uterine contractions with progressive effacement and dilatation of the cervix. Consider use of oral tocolytics and magnesium sulphate infusion, where appropriate.
- Confirmed prelabour rupture of membranes demonstrated by direct visualisation of pooling liquor on speculum examination.
- Positive fetal fibronectin
- Significant antepartum haemorrhage
- Severe pre-eclampsia or uncontrollable hypertension
- Elective Caesarean section prior to 39 weeks
- Other maternal or fetal conditions that make preterm delivery (spontaneous or iatrogenic) likely.
- Women with fetal growth restriction at risk of spontaneous or iatrogenic preterm delivery

Women admitted at 22+5 weeks gestation, after discussions between the consultant obstetrician and consultant neonatologist, and subsequently with the mother, a decision may be made to give steroids. The neonatal team would still not necessarily plan to attend delivery until greater than (>)23/40.

Consider steroid administration between 34 and 36 weeks of pregnancy, especially if Caesarean section is likely.

Treatment

For women between 22+5 and 23+6 weeks of pregnancy who are in suspected or established preterm labour, are having a planned preterm birth or have PPROM:

Antenatal corticosteroids are most effective when the course is completed 24 hours to 7 days prior to delivery. Optimum timing of administration is therefore of paramount importance, and steroids should not be given “just in case”.

> Corticosteroid treatment is associated with a reduction in respiratory distress syndrome (RDS), cerebroventricular haemorrhage, necrotizing enterocolitis (NEC) and an overall lower rate of death and neurodevelopmental impairment at 18-22 months. Discuss with the woman (and her family members or carers as appropriate) the use of antenatal corticosteroids in the context of her individual circumstances.

A Consultant Obstetrician and Neonatologists should be involved in discussion and decision making with the mother. If the parents decide the baby is not to be resuscitated if delivered then antenatal corticosteroids are not indicated. See Section F– Extremes of Viability (also see flow chart on p 5 of the guideline)

- **Consider** antenatal corticosteroid therapy between 22+5 and 23+6 weeks. Therapy is associated with a lower rate of death and neurodevelopmental impairment at 18-22 months.

- Discuss with the woman (and her family members or carers as appropriate) the use of antenatal corticosteroids in the context of her individual circumstances.
- Consultant Obstetrician and Neonatologists should be involved in discussion and decision making with the mother.
- If the parents decide the baby is not to be resuscitated if delivered then antenatal corticosteroids are not indicated. See Appendix F – Extremes of Viability(flow chart at start of the guideline)
- Offer antenatal corticosteroids between 24+0 and 33+6 weeks of pregnancy for women who are in suspected or established preterm labour, are having a planned preterm birth or have PPROM.
- Consider antenatal corticosteroids for women between 34+0 and 35+6 weeks of pregnancy who are in suspected, diagnosed or established preterm labour, are having a planned preterm birth or have PPROM.

A course of corticosteroids should be given for

- Elective / semi-elective caesarean delivery planned **before 39+0 weeks** to reduce the risk of transient tachypnea of the newborn and respiratory distress syndrome.
- Where appropriate, caesarean delivery should be planned for 39+0 onwards to reduce respiratory morbidity. The risk of RDS requiring NICU admission is 4% at 38 weeks and only 1% at 39 weeks.
- These criteria apply to both singleton and multiple pregnancies.

If there is any doubt as to the appropriateness of administration of corticosteroids this should be discussed with the Consultant Obstetrician

A careful steroid history should be taken from women who are transferred from other units antenatally, to ensure that an appropriate steroid regime is completed but not duplicated.

The neonatal team should be informed of any emergency admission that requires antenatal corticosteroid therapy.

Dose regimen

Two doses of betamethasone 12mg should be given by intramuscular injection at 12-24 hours interval, depending on the likely time scale of delivery. The two doses are a complete course of treatment.

If there is a supply problem with betamethasone then dexamethasone is an acceptable alternative, (see appendix 2).

Timing of administration

- Antenatal corticosteroids have the greatest effect in reducing respiratory distress syndrome (RDS) 24 hours after the administration of the second dose and within 7 days.
- Steroid doses should still be given even if delivery is anticipated within 24 hours of administration, as there is reduction in the rate of neonatal death.
- There is no evidence of benefit for reducing morbidity or mortality if delivery occurs after 7 days from steroid administration and therefore treatment should not be indiscriminate.

Repeat doses

Repeated courses of antenatal corticosteroids are not currently routinely recommended as they have been associated with reduced birth weight and head circumference. A Cochrane review showed short term benefit for babies. There was a lower incidence of respiratory distress and fewer serious health problems in the first few weeks of life for women having a second round of steroids if initial course was over 7 days previous. However, animal studies have suggested potential adverse effects such as developmental delay, necrotizing enterocolitis, maternal and neonatal sepsis.

A repeat course might be considered if an initial course was given at less than 26+0 weeks and another obstetric indication for delivery occurs later in the pregnancy, as there is limited data regarding evidence for benefit of corticosteroid administration at less than 26 weeks. This should be an Obstetric Consultant decision in discussion with the consultant Neonatologist. Concerns over repeated doses are greater for Dexamethasone than Betamethasone.

Diabetes mellitus
Diabetes mellitus is not a contra-indication for steroid administration. However, control of diabetes may be more difficult when corticosteroids are used.

This is covered by Portsmouth Hospital University NHS Trust guideline: Diabetes Pregnancy Management, which anticipates that mothers should be admitted for at least 24 hours (usually to the antenatal ward) to ensure monitoring at the time when betamethasone will be having its maximal effect on elevation of blood glucose levels. Careful glucose monitoring by the woman following discharge is also recommended since continuing effects of betamethasone may be evident for up to 48 hours requiring additional subcutaneous insulin.

Cautions
Caution should be exercised in antenatal corticosteroid administration in women with systemic infection including sepsis or tuberculosis due to the potential suppression of the immune response to infection.

Caution should be exercised if contemplating delay of delivery for steroid prophylaxis in cases of overt chorioamnionitis and consultant opinion should be sought. The harmful effects of chorioamnionitis likely outweigh the beneficial effect of antenatal steroids and so delivery should not be routinely delayed. Corticosteroids can still be given without delaying delivery.

SECTION D: TOCOLYSIS
Tocolysis is indicated when a patient presents in threatened or actual preterm labour in an attempt to delay delivery for administration of antenatal corticosteroids, magnesium sulfate or for in utero transfer to a unit with an appropriate level Neonatal Unit. It should not be used if steroids have previously been given and magnesium sulfate is not indicated.

Longer term follow-up studies of exposure to nifedipine suggest that it is safe for the neonate even when it is used in the first trimester.

Importantly, nifedipine is used off-licence for this indication.

Dose regimen
There is no consensus about the appropriate regimen for nifedipine.

If the decision is made for tocolysis by an Obstetric Registrar or Consultant. The suggested dose of nifedipine is;

- An oral loading dose of 20mg using an immediate release preparation
- Maintenance dose, starting 6 – 8 hours post loading dose – 10mg three times a day
- Dose can be increased to 20mg four times a day adjusted to uterine activity
- Daily doses of 60mg and above are associated with an increase in side effects
- Maximum duration of treatment is 48 hours

Side effects
Hypotension (in normotensive women the effect on blood pressure seems to be small and seldom severe enough to withdrawal treatment (Ferguson 1989)

- Tachycardia
- Palpitations
- Peripheral oedema
- Headaches
- Facial flushing.
- Women with PTL may typically complain of facial flushing and mild headache
- Less common effects are constipation, dizziness, nausea, bradycardia, fatigue, rash and increased liver enzymes (which does not result in long term liver disease).

Nifedipine Contraindications

- Cardiac conducting defects
- Hypotension
- Left ventricular failure
- Hepatic and renal failure are relative contraindications

Cautions
Women taking medicines that may interact with nifedipine (see BNF appendix 1 [calcium channel blockers] for more detail).
Avoid grapefruit juice.

Nifedipine use with magnesium sulfate
In the late 1980's and 1990's there were occasional reports of profound hypotension, maternal death and neuromuscular blockade resulting from the combined use of nifedipine and magnesium sulfate. More recent clinical experience however suggests that these agents can safely be used together (Papatsonis 2000).

If significant muscle weakness occurs during magnesium sulfate infusion in women who are also receiving nifedipine the magnesium infusion should be stopped immediately. Symptoms should improve within 15-30mins.
Calcium gluconate 1 gram or calcium chloride 10 mgs can also be given of there is profound cardiovascular or respiratory collapse.

Nifedipine - Neonatal Effect and Breastfeeding
Nifedipine is rated Category C (teratogenic potential is uncertain and should only be used when the maternal benefits outweigh potential fetal side effects). No specific congenital defects in humans have been recorded that are attributable to its use in the correct dosage (see above) and despite extensive experience with its use.

Whilst nifedipine is excreted in breast milk in doses equivalent to serum levels it is considered safe for breast feeding mothers to continue this medication if required for the control of blood pressure (American Academy of Paediatrics, 1994).

SECTION E: MAGNESIUM SULFATE

Less than 33+6 weeks gestation with anticipated delivery within 24 hours

Is urgent delivery necessary due to suspected maternal or fetal compromise?
(e.g. severe fetal distress, antepartum)

YES

NO

Expedite Delivery.

Do NOT delay delivery to

administer magnesium sulfate

Discuss with Obstetric Registrar/Consultant Counsel patient about magnesium sulfate for fetal neuroprotection.

Administration of magnesium sulfate confers benefit even if delivery is anticipated within 4 hours

Administer magnesium sulfate infusion at dosage of:

- **Loading Dose**: 4g IV over 20 minutes via infusion pump
- **Maintenance Dose:** 1g IV per hour for 24 hours or until delivery.

Irrespective of:

- Singleton or multiple pregnancy
- Mode of delivery
- Reason for preterm birth
- Whether or not antenatal steroids have been administered

Maternal Monitoring (for uncomplicated maternal condition, eg not severe PET) on MEOWS:

- Urine output monitoring
- Hourly respiratory rate
- 2 hourly blood pressure
- Reflexes and Consciousness (AVPU Score) assessed 4-6 hourly

Fetal Monitoring:

- In the absence of complications fetal monitoring should be undertaken 6-8 hourly

Continue magnesium sulfate until delivery or for a maximum of 24 hours unless:

- The woman becomes hypotensive
- Respiratory rate decreases below 12 breaths/min
- Urine output less than 100ml for 4 hours
- Tendon reflexes are absent

If magnesium sulfate overdose suspected:

- Stop infusion.
- Contact Registrar/Consultant
- Send bloods for renal function and magnesium levels.
- Consider IV 10mls 10% calcium gluconate

Management of Mother who has received Magnesium Sulfate ($MgS0_4$)- Flowchart [PReCePT 2020 95%]

The responsible midwife at birth should inform the Neonatal team that the mother has been receiving magnesium sulfate

Babies born preterm are at increased risk of cerebral palsy, with 25% of all cases occurring in children born before 34 weeks gestation. Evidence suggests that the administration of Magnesium Sulfate to mothers in preterm labour reduces the incidence of cerebral palsy in their children. Before 30 weeks gestation it is estimated that 46 women would need treatment to prevent one case of cerebral palsy. Between 30 and 34 weeks the number needed to treat rises to 56. Unlike steroids this protective effect occurs within a short time of the administration of magnesium sulfate.

Indication

- Treatment should be offered to women at less than 33 weeks and 6 days gestation when preterm birth is planned or expected within 24 hours.
- Magnesium sulfate should be offered irrespective of the indication for premature delivery, the number of fetuses carried, whether steroids have been given, mode of delivery and parity (unless the mother has decided that she does not wish for neonatal resuscitation at deliveries less than 24/40).
- **Urgent delivery should not be delayed to administer magnesium sulfate**.

Magnesium sulfate should be administered for at least four hours before birth but it is still thought to be beneficial if given later than this.

Contraindications

- There are no absolute contraindications to the administration of magnesium sulfate for preterm delivery
- Maternal hypotension is a relative contraindication and may be exacerbated by concurrent use of calcium channel blockers such as nifedipine due to their synergistic effects.
- Significant antepartum haemorrhage or suspected abruption are also a relative contraindication due to its tocolytic effects.

Dose and timing of administration

Magnesium sulfate should be given intravenously

- 4 gram loading dose (over 20 minutes)
- 1 gram per hour maintenance dose via intravenous route, with no immediate repeat doses.
- Continue regimen until birth or for 24 hours, whichever comes first.

Please record the name and gestation of the patient in the magnesium sulfate book in the drug cupboard when you remove it, as the use of this product is monitored by Pharmacy.

Repeat doses

If magnesium sulfate was last given more than six hours ago **and** preterm birth (less than 34 weeks' gestation) again appears inevitable within 24 hours, a repeat dose may be considered.

Monitoring

During administration of intravenous magnesium sulfate, women should be monitored regularly and recorded on Modified Early Obstetric Warning (MEOWS) and resuscitation and ventilatory support should be available immediately if needed.

Before and after loading

A minimum assessment should include checking pulse, blood pressure, respiratory rate and patellar reflexes before loading dose, and at 10 and 20 minutes after loading dose infusion has started. These should all be assessed, along with urine output, at least every four hours.

Maintenance dose

Magnesium sulfate infusion can be continued provided that:

1. The knee jerk reflex is not abolished (beware if woman has an epidural)
2. Urine output remains greater than (>) 30 ml/h

   Magnesium sulfate is excreted by the kidneys.
3. SpO_2 is maintained above 95%
4. Respiratory rate does not fall below 10 breaths per minute.
5. Diastolic blood pressure does not fall more than 15 mm Hg below baseline level.

If any of these criteria are present inform Obstetric registrar. If the knee jerk reflex is abolished, stop the infusion immediately and summon the Obstetric and Anaesthetic Registrars urgently.

In this circumstance the midwife should send blood for immediate serum magnesium levels.

Women on magnesium sulfate therapy should have the above observations recorded on the Modified Obstetric Early Warning (MOEWS) chart by the midwifery staff every 4 hours

Magnesium levels:

Routine measurement of magnesium blood levels is unnecessary. If measured, therapeutic magnesium levels are thought to be in the range of 1 - 3.5 mmol/l.

Level	**Effect**
Greater than 3.5 mmol/l	Abolition of knee jerk
5-7.5 mmol/l	Respiratory arrest
Greater than 15 mmol/l	Cardiac arrest

Indications for measuring magnesium levels include:

1. Reduced renal function (e.g. urine output less than 30mls/hour, creatinine greater than 90)
2. Signs of toxicity (e.g. absent patellar reflexes)
3. Unexplained clinical symptoms or signs
4. SpO_2 is below 94%.
5. Respiratory rate below 10 breaths per minute

Fetal Monitoring

Continuous cardiotocograph (CTG) is strongly recommended during magnesium sulfate infusion in a fetus of 26 weeks gestation and above.
Interpretation of the CTG should take into account the reduced variability that is often seen with magnesium infusions

Toxicity

For women on magnesium sulfate, monitor for clinical signs of magnesium toxicity at least every 4 hours by recording pulse, blood pressure, respiratory rate and deep tendon (for example, patellar) reflexes. [NICE 2019]

Magnesium toxicity is unlikely with the regimens recommended in this guideline and serum magnesium concentrations do not need to be routinely measured (RCOG 2006).

However, in women with renal compromise, serial serum magnesium monitoring is recommended 6 hourly.

In cases of suspected toxicity with absent patellar reflex, if the reflex does not return within 1 hour of stopping the magnesium infusion, or respiratory depression is observed, call it warrants a **2222 Maternity Crisis Call** to obtain the appropriate staff in this emergency**.**

Administer intravenous calcium gluconate 1g (10 ml of 10% solution) over 3 minutes to reverse the effects of magnesium sulfate.

Peri-partum
Before delivery, inform the neonatal team that magnesium sulfate was used as it is important it is recorded on Badgernet.
.
Maintain a fluid balance chart for 24 hours after cessation of magnesium sulfate.

Interactions
Magnesium sulfate may interact with nifedipine, causing hypotension. If so, the infusion should be discontinued.In utero transfer

Because of the small risk of respiratory suppression, magnesium sulfate should not be used during transfer between hospitals unless resuscitation and ventilatory support are immediately available.

SECTION F: PRETERM PRELABOUR RUPTURE OF MEMBRANES (PPROM)

Preterm prelabour ruptured membranes (PPROM) occurs in 3% of pregnancies. Its exact aetiology is not fully understood, but thought to be secondary to pathological events such as subclinical infection, bleeding or overdistension of the uterus. The balance of reducing infection risk with allowing advanced gestational age can be a challenge. Approximately 50% of women with PPROM < 37/40 will delivery in the next 5 days.

Obstetric input should be sought.
Management can either be expectant or active, in early planned birth. The main risk with PPROM is infection.

The diagnosis of preterm pre-labour rupture of the membranes is best achieved by maternal history followed by a sterile speculum examination (Carroll 2006). The speculum examination should demonstrate pooling of fluid in the posterior vaginal fornix.

Ultrasound examination is useful in some cases to help confirm the diagnosis.

Digital vaginal examination in the absence of contractions should be **avoided** due to possible introduction of infection.

If a woman has preterm pre-labour rupture of membranes, induction of labour should not be carried out before **37 weeks** unless there are additional obstetric indications (for example, infection or fetal compromise, and there is an available neonatal cot). This is in line with RCOG recommendations. A recent Cochrane review (2017) showed that there was no difference in neonatal infection between those managed expectantly or actively prior to 37 weeks. Early planned birth was however associated with significantly increased neonatal mortality and morbidity, such as NICU admission and respiratory distress syndrome of the neonate, and Caesarean section and endometritis for the mother. Planned early birth did reduce the rates of chorioamnionitis, and led to a shorter hospital stay for the mother.

In women with PPROM with no other indications for early planned birth, mother and baby had better outcomes with expectant management.

If women are diagnosed with PPROM, (less than 37 weeks) the following should be carried out:

- Women should be admitted to hospital
- Presentation should be confirmed, if necessary by ultrasound scan.
- Women should be observed for signs of clinical chorioamnionitis at least 12-hourly.
- Maternal temperature, pulse and fetal heart rate auscultation should be carried out every 6 hours if an inpatient to observe for signs of infection
- Fetal heart cardiotocograph (CTG) should be performed if the woman reports any changes e.g. abdominal pain, reduced fetal movements
- A weekly vaginal swab and at least a weekly maternal full blood count should be considered.
- Fetal monitoring using cardiotocography should be considered where regular fetal surveillance is required. (NICE 2008)

Antibiotics

Erythromycin (250 mg orally 6 hourly) should be given for 10 days following the diagnosis of PPROM

Biophysical profile scoring or Doppler velocimetry **should not be** considered as first-line surveillance or diagnostic tests for fetal infection.

If maternal pyrexia (above 37.8ºC), offensive vaginal discharge or fetal tachycardia is presented – request an urgent obstetric review due to possible diagnosis of chorioamnionitis.

Co-amoxiclav is not recommended for women with PPROM because of concerns about necrotising enterocolitis in the preterm infant.

Any woman laboring < 37/40 should receive intrapartum antibiotic prophylaxis against group B Streptococcus. Benzylpenicillin is recommended. In penicillin allergy, a cephalosporin should be used. In severe penicillin allergy, use vancomycin. Clindamycin is not recommended.

Steroids

A course of antenatal corticosteroids should be administered following the diagnosis of PPROM if the gestation is <35/40, or if <39/40 and the patient is likely to need delivery by Caesarean section (eg breech, IUGR).

Tocolysis

Use of tocolysis in PPROM is controversial. Women with PPROM and uterine activity who require intrauterine transfer or antenatal corticosteroids should be considered for tocolysis and discussed with Obstetric Consultant.

Recommendation on pre-labour rupture of membranes with meconium

The presence of meconium predisposes to infection. However it is also worth considering if the pigment could be secondary to decidual haemorrhage instead. These patients should be examined for possible chorioamnionitis, but meconium stained fluid in PPROM alone is not an absolute indication for delivery.

SECTION G: EXTREMES OF VIABILITY – 22+6 to 26 weeks

Gestational age weeks	Team Involvement **Obstetric Team** Registrar ST6/7 Consultant	Team Involvement **Neonatal team** Registrar or Consultant	Attend at delivery	MgSO4	Steroids	Mode of Delivery
22-22+6/40*	YES	NO. Inform Neonatal team**	YES	NO	YES	Vaginal
23-23+6/40	YES	YES	Neonatal team Obs team	YES	YES	Vaginal
24-24+6/40	YES OBS REG/CON	YES	Neonatal team MW &obs Reg Obs Consultant For breech	YES	YES	Vaginal
25/40	YES OBS REG/CON	YES	Neonatal team MW & Reg Obs Consultant For breech/ LSCS	YES	YES	Vaginal/LSCS **After counselling** by senior obstetrician and neonatologist
Uncertain	YES OBS REG/CON	Yes	Yes	YES	YES	MW/REG Try to establish the gestational age (scan may help) Vaginal/ LSCS **After appropriate senior counselling**

Neonatal involvement

* As the neonatal team plan to usually offer active resuscitation from 23+0 weeks, steroids would be needed from 22+5 and magnesium sulfate from 22+6, we would still caution parents that despite giving these interventions, resuscitation may still not be appropriate or possible.

** Neonatal team should be informed of admissions at 22 weeks but would not normally consider seeing parents until about 22+5

- When the team are in attendance at a birth; the NICU team will prepare their working environment and ensure that the resuscitaire and equipment are ready for immediate use. It is essential that all pre-term babies less than 30 weeks should be placed on the resuscitaire on a covered Transwarmer after birth and wrapped in towels as opposed to the use of plastic bags.
- It is currently accepted that survival prior to 22 weeks and 6 days gestation is very unlikely.
- At 24 weeks it is also accepted that full active resuscitation and management should be offered, except in exceptional circumstances.
- Although resuscitation would not normally be offered before 23 weeks, decisions regarding Obstetric and Neonatal intervention at the extremes of viability should be consultant led and discussed with the parents and a joint decision made and recorded in the hand held notes

Survival rates for extremely premature infants continue to improve. However morbidity rates with health problems such as cerebral palsy, chronic lung disease and retinopathy persist. Adequate counselling of

women at risk of delivering at the viability threshold is paramount, and optimizing obstetric care will provide a neonate in as good condition as possible for the waiting neonatal team.

Survival to discharge home for inborn babies 2010-2016 (PHT NICU results):

	23 (n=47)	24 (n=67)	25 (n=73)	26 (n=76)	27 (n=96)	28 (n=136)	29 (n=117)
No. delivered at this gestation	47	67	73	76	96	90	90
Born alive	67%	80%	80%	83%	98%	95%	99%
Admitted to NICU	67%	86%	80%	84%	99%	95%	100%

- Gestational age is the biggest determinant of primary outcome,
- Birthweight and female sex independent positive associations with survival, with the best rates between birthweight centiles 50 and 85.
- Between 23 and 28 weeks, each additional day in utero confers a 3% survival benefit.

Corticosteroids

- Administration is a consultant decision jointly with the parents; the joint plan must be documented in the hand held notes.
- All women at risk of imminent delivery between 23 to 25+6 weeks gestation should receive a course of antenatal steroids
- Antenatal corticosteroid therapy between 23 and 26 weeks was associated with a lower rate of death and neurodevelopmental impairment at 18-22 months.

Administration of corticosteroids should be discussed with the neonatal team, mother, partner and family if appropriate.

Documentation of dates the steroids were given should be clearly written in the notes under “Obstetrician’s Information” on the Obstetric History Summary page for ease of reference.

If the baby is not for active resuscitation, antenatal corticosteroid administration is not indicated. Documentation of dates the steroids were given should be clearly written on the extremes of viability proforma.

Antibiotics

Prematurity is a risk factor for early onset Group B Streptococcus disease of the neonate. A recent NICE 2017 review concluded that intravenous antibiotics (usually benzylpenicillin or clindamycin) should be administered to all women in active preterm labour. **See Trust guideline for further information.**

http://pht/Departments/Maternity/Maternity%20Services%20Guidelines/Group%20B%20Streptococcus-Guideline.doc

Magnesium sulfate

Evidence for magnesium sulfate is lacking for extremely premature infants. The RCOG suggest that if active management is to be used, it would be logical to offer neuroprotective magnesium sulfate.

Mode of delivery
Aim for vaginal birth on most occasions. If the baby is breech, or the patient has had previous Caesarean section(s), Caesarean delivery may be indicated or considered after discussion with the patient by a senior clinician.

Fetal Monitoring
CTG is extremely difficult if not impossible to interpret prior to 26 weeks' gestation. Decisions regarding intermittent auscultation +/- CTG in labour need to be discussed with consultant obstetrician, and whether intervention for presumed fetal distress would be appropriate depends on the individual clinical circumstance. Management plan needs to be clearly documented in the notes.

1. INTRODUCTION

In the UK, approximately 8% of babies are born before 37 completed weeks ("preterm") Babies born preterm are at a higher risk of mortality: 42/1000 live births compared to 5/1000 live births overall. For babies below 32 weeks, mortality in the first year of life was 14/1000 live births compared to 1.8/ 1000 births in babies of 30-41+6 weeks gestation. Most preterm births are greater than 28 weeks gestation but 0.6% are between 22 and 28 weeks.

Prevention and treatment of preterm birth has an impact upon not only the individual and family but the health economy as a whole. Gestation and birthweight are the two most important factors in determining outcome. Prematurity can lead to a multitude of medical complications such as respiratory distress syndrome (RDS), necrotising enterocolitis and cerebral palsy amongst many others. The cost of neonatal care often rises to tens of thousands of pounds per case, notwithstanding the long term (often lifelong) impact and costs. The psychological trauma for families affected by preterm birth and prolonged hospital admission should not be forgotten.

75% of preterm births are spontaneous, whilst 1 in 4 are delivered for medical reasons such as pre-eclampsia or growth restriction. Spontaneous preterm labour is multifactorial in origin, can involve infection (20-40%), uterine over-distension and cervical abnormalities. Identifying mothers at risk of preterm birth may allow up to 15% of births to be prevented or delayed towards later gestations, improving outcome for mother and baby. The Preterm Birth surveillance clinic provides assessment and appropriate treatment of high and intermediate risk women.

Preterm premature rupture of the membranes (PPROM) introduces significant risk of ascending genital tract infection, which can lead to chorioamnionitis and morbidity of both mother and baby. The guideline will cover its diagnosis, treatment, and discuss the balance between allowing advancing gestation and minimising risk of infection.

Mothers who present with threatened preterm labour can be screened using the bedside test fetal Fibronectin (fFn). A negative result allows reassurance that labour is not imminent, and will minimize the use of resources such as steroids, tocolysis and admission to hospital.

The use of magnesium sulfate has been recommended to reduce the risk of premature babies developing cerebral palsy. Currently we recommend its use if delivery is expected within 24 hours under 30 weeks gestation, and consider between 30 and 34 weeks

Decisions regarding obstetric management of patients at the extremes of viability are complex. The guideline will cover the process for these decisions and provide a proforma for completion. Senior input is key from as early as possible, preferably from a dedicated Preterm Birth Consultant

Portsmouth Hospitals NHS Trust (PHT) has a level 3 neonatal intensive care unit (NICU) and as such will have a high level of transfer for premature pregnancies.

2. SCOPE

All staff (permanent, locum, agency, bank and voluntary staff of the Trust, the Ministry of Defence Hospital Unit, Joint Hospitals Group South (Portsmouth) and Engie must follow the procedural documents agreed by the Trust. For staff other than those directly employed by the Trust the appropriate line management or chain of command will be taken into account. Breaches of adherence to Trust policy may have potential contractual consequences for the employee.

In the event of an infection outbreak, pandemic or major incident, the Trust recognises that it may not be possible to adhere to all aspects of this document. In such circumstances, staff should take advice from their manager and all possible action must be taken to maintain ongoing patient and staff safety.

3. PROCESS

Currently 5 separate guidelines exist covering premature birth. This guideline will amalgamate all the information and aim to make it easier to find pertinent points to assist in the management of these complex pregnancies.

Preterm labour – labour prior to 37 weeks gestation
Preterm birth – delivery prior to 37 weeks gestation

Abbreviations

ANC – Antenatal Clinic
CTG – Cardiotocograph
GBS – Group B Streptococcus
HVS – High Vaginal Swab
LLETZ – Large loop excision of the Transformation Zone
LSCS – Lower Segment Caesarean Section
MSU – Mid stream Urine sample
NICE – National Institute for Health and Clinical Excellence
NICU- Neonatal Intensive Care Unit
PPROM – preterm pre-labour rupture of the membranes. Rupture of the membranes prior to 37 weeks and over 24 hours before labour begins.
PTB – Preterm birth
RCOG – Royal College of Obstetricians and Gynaecologists
RDS – Respiratory distress syndrome
TVUS – Trans Vaginal Ultrasound
US- Ultrasound

4. TRAINING REQUIREMENTS

Doctors working in maternity will complete training for undertaking the fetal fibronectin test.

Midwives caring for women on magnesium sulfate infusions will have training to identify deep reflexes

5. REFERENCES AND ASSOCIATED DOCUMENTATION

National Institute for Care and Health Excellence (2019) Preterm labour and birth (NICE guidelines 25) Available at https://www.nice.org.uk/guidance/ng25 (Accessed 1st September 2020)

Stutchfield P, Whitaker R, Russell I; Antenatal Steroids for Term Elective Caesarean Section (ASTECS) Research Team. Antenatal betamethasone and incidence of neonatal respiratory distress after elective caesarean section: pragmatic randomized trial. BMJ 2005;331-662

Portsmouth Hospitals NHS Trust. Diabetes Pregnancy Management.

British National Formulary and Specification of Product Characteristics for further information www.medicines.org.uk

6. EQUALITY IMPACT SCREENING

The Trust is committed to ensuring that, as far as is reasonably practicable, the way we provide services to the public and the way we treat our staff reflects their individual needs and does not discriminate against individuals or groups on any grounds.

This procedural document has been assessed accordingly. The assessment document is held centrally and is available by contacting the Governance Co-ordinator.

7. MONITORING COMPLIANCE

In order to provide Maternity Services with assurance of implementation of the guideline and the provision of safe clinical care the following process of monitoring will be utilised.

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This procedural document will be monitored to ensure it is effective and to provide assurance of compliance.

Element to be monitored	Lead	Tool	Frequency of Report	Reporting arrangements	Lead
Audit Identifiers below	Obstetric Audit lead	**Maternal Notes**	Ongoing prospective audit/data collection	Guideline audit report to: Maternity Governance Forum	Operation Matrons with Obstetric Governance Lead
Correct use of steroid and magnesium in preterm birth	ATAIN Midwife	**Maternity Notes**	Ongoing – reporting nationally via Trust	Report to Trust and LMS Shared via maternity Governance Forum	ATAIN Midwife

Audit questions:

- There is documented evidence that women with PROM have been given choice with regards to active or expectant management
- A plan of care regarding IOL/expectant management is made and documented in the clinical notes
- There is documented evidence of obstetric input for women 34 – 36+6 weeks with PPROM, and evidence of a plan of care.

- Preterm births having steroids administered and magnesium as per guidance (time allowing)
- Extremes of viability forms used in all cases under 22+6 onwards and completed correctly.

Appendix A: Roles and responsibilities

Community midwives are responsible for identifying patients at risk of preterm birth and referring them to the Preterm Clinic. Referral criteria for the Preterm Clinic are in Section A.

Obstetricians are responsible for the diagnosis of threatened / actual preterm labour, preterm pre-labour rupture of the membranes (PPROM), prescriptions of drugs as required and liaising with the multidisciplinary team including neonatal intensive care unit (NICU) staff.

Hospital midwives are responsible for communicating patients in threatened preterm labour to the Obstetricians, and administering medications as prescribed

Portsmouth Hospitals University NHS Trust

Appendix B: Proforma for management decisions at the extremes of viability (22+6 onwards)

Mothers DETAILS/STICKER

Date/Time of consultation:	Gestation by USS.	EDD	Named Lead Consultant

Current antenatal problems:		
		SROM: Date: Time:
Parents counselled by neonatologists?	Yes/No Date/Time:	Detail:
Neonatologists to be present at delivery?	Yes/No	
Steroids (to be discussed with neonatal team)	Yes/No Date/Time: Gestation given:	
MgSO4	Yes/No Details:	
Fetal surveillance? (IA/CTG)	Yes/No	Detail
Mode of delivery if labour commences	Vaginal	Rationale:
	Caesarean	

Must be completed by a Senior SpR 6-7/Consultant and be reviewed as part of the daily patient review

Consultant review should take place within 14 hours

Form completed by:

Date: Time: Signed:

*Review date due at _____ weeks on _____

*Please complete a new form for each review.

Obstetric Discussion
(To include parent's preferences)

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Appendix C: Basic Drug Information

Please refer to British National Formulary and Specification of Product Characteristics for further information www.medicines.org.uk

BENZYLPENICILLIN

Indication: prophylactic antibiotic cover in labour against GBS

Administration: Intravenous injection: 3g as soon as possible after the onset of labour and then 1.2g 4hourly until delivery

Contra-indications: penicillin hypersensitivity

Adverse Effects: hypersensitivity reactions including urticaria; fever; joint pains; rashes; angioedema; anaphylaxis; serum sickness – like reaction

BETAMETHASONE

Indications: preterm labour for the maturation of fetal lungs

Administration: 12mg intramuscular injection two doses 12 hours apart

Contraindications: Systemic infection

Adverse Effects: Dyspepsia, abdominal distension, candidiasis and hyperglycaemia;

CALCIUM GLUCONATE

Indications: Reversal of Magnesium Sulfate toxicity

Administration: 1 g of Calcium Gluconate (10 mL of 10% solution) IV slowly over 10 minutes

Contraindications: Conditions associated with hypercalcaemia or hypercalciuria (e.g. some forms of malignant disease)

Adverse Effects:,Hypercalcaemia;arrhythmias;Circulatory collapse; feeling hot; hyperhidrosis; hypotension; vasodilation; nausea; vomiting;

CLINDAMYCIN

Indication: Prophylactic antibiotic therapy for GBS in women with penicillin allergy only

Administration: Intravenous infusion: 900mg in 100 ml sodium chloride 0.9%. To be administered over a period of 30 minutes by intravenous infusion and then 8 hourly until birth of baby

Contra-indications: diarrhoeal states

Adverse Effects: diarrhoea; abdominal discomfort; oesophagitis; oesophagael ulcers; taste disturbances; nausea; vomiting; antibiotic associated colitis; leucopenia; rash; pruritis; uricaria; anaphylactoid reactions

DEXAMETHASONE – to be used when Betamethasone is not available

Indications: preterm labour for the maturation of fetal lungs

Administration: 11.4mg intramuscular injection two doses 12 hours apart

Contraindications: Systemic infection

Adverse Effects: Dyspepsia, abdominal distension, candidiasis and hyperglycaemia;

MAGNESIUM SULFATE

Indication: Neuroprotection of the baby

Loading dose

4 g (16 mmoL) IV slowly over 20 minutes.

Using a 20 mL syringe draw up 20mL of 20% magnesium sulfate. This contains 4g (16 mmoL) of magnesium sulfate

Give at a rate of 1 mL/min.

Maintenance infusion

a) Infusion preparation

- Using a 50 mL syringe draw up 50mL of 20% magnesium sulfate. This provides a concentration of 200 mg/mL.

b) Administration

- Infuse at 1 g/hr i.e. infusion rate of 5 mL/hr

The infusion should be stopped immediately if the woman's knee jerk reflex is abolished or if respiratory depression is observed.

Contraindications

- Hepatic impairment

Adverse effects

Nausea, vomiting, thirst, flushing, hypotension, respiratory depression, loss of tendon reflexes, muscle weakness.

Antidote

If the knee jerk tendon reflex is lost and does not return within 1 hour of stopping the magnesium infusion, or respiratory depression is observed (less than 10 breaths per minute), immediately call the obstetric registrar & labour ward anaesthetist. Administer 1 g of Calcium Gluconate (10 mL of 10% solution) IV slowly over 10 minutes.

Magnesium therapy will usually cease after 24 hours following a consultant review.

NIFEDIPINE

If the decision is made for tocolysis by an Obstetric Registrar or Consultant. The suggested dose of nifedipine is;

- An oral loading dose of 20mg using an immediate release preparation
- Maintenance dose, starting 6 – 8 hours post loading dose – 10mg three times a day
- Dose can be increased to 20mg four times a day adjusted to uterine activity
- Daily doses of 60mg and above are associated with an increase in side effects
- Maximum duration of treatment is 48 hours

Paracetamol may be administered (in view of the headache commonly associated with nifedipine).

Side effects

Hypotension (in normotensive women the effect on blood pressure seems to be small and seldom severe enough to withdrawal treatment (Ferguson 1989)
Tachycardia, Palpitations, Peripheral oedema, Headaches, Facial flushing, Women with PTL may typically complain of facial flushing and mild headache
Less common effects are constipation, dizziness, nausea, bradycardia, fatigue, rash and increased liver enzymes (which does not result in long term liver disease).

Contraindications

Cardiac conducting defects, Hypotension, Left ventricular failure, Hepatic and renal failure are relative contraindications.

Cautions

Women taking medicines that may interact with Nifedipine (see BNF appendix 1 [calcium channel blockers] for more detail).
Avoid grapefruit juice.

PARACETAMOL

Indications: analgesia

Administration: 1 gram (500mg if less than 50kg)orally every 4- 6 hours no more than 8 tablets in 24 hours – Consider maternal weight and dose accordingly

Contraindications:

Adverse Effects: Rare Thrombocytopenia, agranulocytosis, bronchospasm, hepatic function abnormal, severe cutaneous adverse reactions (SCAs)