Threatened Preterm Labour Including Fetal Fibronectin and Tocolytic Clinical Practice Guideline

Guideline Number:	648	Supersedes:	N/A	Classification	Clinical

Version No:	Date of EqIA:	Approved by:	Date Approved:	Date made active:	Review Date:
1	2.1.2018	Obstetrics and Gynaecology Written Documentation Group	17/12/2018	17/12/2018	17/12/2021
		Obstetric Group - Extended whilst review is finalised	08/02/2022	09/02/2022	08/08/2022

Brief Summary of Document:	The aim of this guideline is to aid diagnosis, investigation and management of threatened preterm labour (TPTL). This guideline only applies to people in threatened preterm labour with intact membranes.
Scope	The guideline applies to obstetricians, midwives, anaesthetists and paediatricians who are caring for a patient who is experiencing threatened preterm labour in any setting.

To be read in conjunction with:	645 - Preterm Labour (Spontaneous Rupture of Membranes) Guideline. 632 - Management of diabetes in pregnancy Guideline 662 - Magnesium Sulphate for Neonatal Neuro-protection Guideline

Owning group	Obstetrics and Gynaecology Written Documentation Group

Reviews and updates		
Version no:	Summary of Amendments:	Date Approved:
1	New Guideline	17/12/2018

Glossary of terms

Term	Definition
FFN	Fetal fibronectin
PPROM	Preterm Prelabour Rupture Of Membranes
TPTL	Threatened Preterm Labour
RDS	Respiratory Distress Syndrome
PTL	Preterm labour
BGH	Bronglais Hospital
EDD	Estimated due date
CTG	Cardiotocograph
MSU	Midstream sample urine
NNU	Neonatal Unit
SpR	Specialist Registrar
BP	Blood pressure
FBC	Full blood count
CRP	C-reactive protein
G&S	Group and save

Keywords	Threatened Preterm Labour, Fetal fibronectin, Tocolytics

Content

1. INTRODUCTION

Spontaneous preterm birth occurs in 7-11% of pregnancies before 37 weeks gestation and in 3 - 4% of pregnancies before 34 weeks gestation.

Births prior 34 weeks of gestation cause most of neonatal mortality and morbidity. The frequency of bronchopulmonary dysplasia, intraventricular haemorrhage, retrolental fibroplasia, neurodevelopmental problems, and cognitive difficulties increases with the grade of pre-maturity.

Incidence of spontaneous preterm birth has not decrease in the last decade, but there is effective management to reduce the associated complications in the infants/foetus. Antenatal steroids significantly reduce morbidity and mortality of the infants/foetus. Timely institution of such treatment depends on accurate prediction of spontaneous preterm birth.

2. SCOPE

The guideline applies to obstetricians, midwives, anaesthetists and paediatricians who are caring for a patient who is experiencing threatened preterm labour in any setting.

3. AIM

The aim of this guideline is to aid diagnosis, investigation and management of threatened preterm labour (TPTL). This guideline only applies to people in threatened preterm labour with intact membranes. It does not apply for preterm labour with preterm, pre-labour rupture of membranes (PPROM). For those instances refer to the HDUHB Guideline 645 - Preterm Labour (Spontaneous Rupture of Membranes)

4. OBJECTIVES

The aim of this guideline will be achieved by the following:

- Identifying the risk factors associated with spontaneous preterm birth
- By safe and timely management of people in TPTL

5. RISK FACTORS ASSOCIATED WITH SPONTANEOUS PRETERM BIRTH

Although the absolute cause of spontaneous preterm birth is difficult to identify in most individual cases, risk factors have been identified and include black ethnicity, vaginal bleeding during pregnancy, low body mass index, anaemia, certain vaginal or urinary tract infections during pregnancy, preterm contractions, multifetal gestation, a short cervix during pregnancy, and a history of a prior spontaneous preterm birth (Table 1). However, approximately 50% of women who deliver preterm do not have identifiable risk factors.

Table 1. The Relationship between Maternal Characteristics and Spontaneous Preterm Birth in Singleton Gestations

Risk factor	Relative risk for spontaneous preterm birth < 37 weeks
Black ethnicity	1.5
Body mass index < 19.8	2.5
History of a previous spontaneous preterm birth	2.7
Preterm contractions	1.8
Vaginal bleeding	1.5
Cervical length ≤ 2.5 cm	3.5
Positive fetal fibronectin test	3.3

Approximately 80% of preterm births are considered to be spontaneous as a result of either preterm labour or preterm, pre-labour rupture of membranes. The remaining 20% are medically indicated preterm births, usually because of pre-eclampsia, intrauterine growth restriction, or other indications. There appear to be 4 major pathways leading to preterm birth, and an understanding is paramount to predicting and ultimately preventing preterm birth.

The four pathways are:

(1) pre-mature activation of the fetal or maternal hypothalamic-pituitary-adrenal axis

(2) decidual or systemic inflammation

(3) decidual bleeding and

(4) pathologic distension of the uterus.

All four of these processes lead to a final common pathway of preterm labour/preterm pre-labour ruptured membranes and spontaneous preterm birth.

6. Screening Tools to Determine Risk for Spontaneous Preterm Birth

Two tools have shown high accuracy in predicting preterm birth; i.e. cervical length measurement by transvaginal ultrasound and fFN testing.

Cervical length measurement

A cut-off of 15 mm for cervical length (three studies, 1266 women, rate of preterm birth within 48h 7.1%) predicted 71.1% (95% CI, 59.5 – 80.9%) of preterm births at < 48h with a specificity of 86.6% (95% CI, 84.6–88.5%).

In women with cervical length of ≤ 15mm, one study found 51% delivered within 7 days. However if the cervical length was ≥ 16mm, only 1% delivered within 7 days.

Administration of progesterone in women with a short (< 15 mm) cervix can decrease the

likelihood of preterm birth at less than 34 weeks gestation by 45%.

Fetal fibronectin (fFN)

Most accurate prediction of spontaneous preterm birth gives cervicovaginal fFN test.

fFN is a glycoprotein found in amniotic fluid, placental tissue, and the extracellular substance of the decidua basalis next to the placental intervillous space. It is thought to be released through mechanical or inflammatory mediated damage to the membranes or placenta before birth.

In normal pregnancy fFN is present in the vagina up to the fusion of the chorionic membrane with the maternal decidua at approximately 20 – 22 weeks of gestation. After this time the level of fFN then falls to below 50ng/ml. After 22 weeks of gestation, a level above 30ng/ml is thought to result from inflammatory or mechanical insult to either the placenta or the fetal membranes indicating separation of the chorion and the deciduas, and imminent delivery. Concentrations ≥50ng/ml during 23 – 35 weeks of gestation have been shown to indicate a greater risk of preterm delivery. Meta-analysis suggests that fFN has a sensitivity of 77% and a specificity of 87% in predicting delivery within 7 days in symptomatic women.

fFN test can predict imminent birth among women with symptoms of threatened spontaneous preterm birth but before advanced cervical dilatation and then antenatal steroids, tocolytics, and in utero transfer may be used accordingly.

Antenatal steroids are most effective in the 2-7 days after they are given.

fFN test is most accurate in predicting spontaneous preterm birth within 7-10 days after testing among women with symptoms of threatened preterm birth before advanced cervical dilatation. After a positive test result 17 symptomatic women at 31 weeks gestation would need to be treated with antenatal steroids to prevent one case of RDS.

If steroids were to be used for all symptomatic women at this gestation without fFN testing than 109 women would be treated with antenatal steroids to prevent one case of RDS.

Table 2. Cervicovaginal Fetal Fibronectin Among Symptomatic Women and Number of Women Needed to Be Treated at 31 Weeks of Gestation With Antenatal Steroids to Prevent One Case of Neonatal Respiratory Distress Syndrome Associated With Spontaneous Preterm Birth Within 7-10 Days of Testing

Test result	Probability of spontaneous preterm birth within 7-10 days of testing (%)	Risk for respiratory distress syndrome at 32 weeks of gestation	Rate of respiratory distress syndrome at 32 weeks of gestation (%)	Number needed to treat
No testing	4.5	0.53	2.0	109
Test positive	20.6	0.53	11.0	17
Test negative	1.0	0.53	0.4	509

7. IMPACT OF FFN TESTING ON PRETERM BIRTH OUTCOMES

Recent data have shown that provider knowledge of fFN results is associated with a lower incidence of preterm birth prior to 37 weeks of gestation. Several studies have also demonstrated a cost savings when fFN testing was used to evaluate women with symptoms of preterm labour. One study from USA demonstrated 40% less admissions with symptoms of preterm labour.

Different studies demonstrated similarly high negative predictive value of fFN test. Honest, et all found that in women symptomatic for preterm labour, a positive test was associated with a 20.6% risk for delivery within 7-10 days of testing, whereas a negative test was associated with a 1% risk for delivery in this interval of time.

A more recent meta-analysis confirmed these findings: a positive test was associated with a 25.9% risk for delivery within the following week, whereas a negative test was associated with a 2.4% risk for delivery within the following week.

Thus, the primary benefit of fFN testing appears to be in its negative predictive value, its ability to identify patients who will not deliver within the following week and in whom interventions and hospitalization may be avoided.

8. INITIAL ASSESSMENT

All women with suspected PTL should be assessed as in-patient.

A full history should be taken, including details on:

- previous obstetric history
- previous medical history
- history of present pregnancy to date including gestational age from agreed EDD
- the start and timing of contractions
- any vaginal loss of blood or fluid
- urinary and bowel symptoms
- symptoms of systemic illness
- history of recent sexual intercourse

Obstetric examination should include:

- abdominal palpation to determine the lie and presentation of the fetus
- symphysial-fundal height
- abdominal ultrasound examination by a trained and competent operator to assess fetal viability, presentation, estimate fetal weight, measure the liquor volume and placental site
- any evidence of uterine, suprapubic or renal angle tenderness
- any palpable uterine contractions

Vaginal examination should then be performed:

- pass a sterile speculum
- look for a pool of liquor, vaginal blood and cervical dilatation
- if appropriate a fibronectin swab should then be taken (see below)
- take swabs from the vaginal fornix (HVS), low vagina (LVS) and endocervical canal (Chlamydia) for infection screen
- if membranes are intact a gentle sterile digital examination can be performed to assess cervical effacement and dilation OR
- transvaginal ultrasound for cervical length if a trained operator available
- digital examination should be avoided if premature rupture of membranes is suspected

Investigations should be performed:

- maternal pulse, BP, temperature and respiratory rate
- CTG (continuous ≥ 26 weeks)
- urine dipstick and MSU
- blood for FBC, CRP, G&S (and blood cultures, if temperature above 37.5^{o}C)

9. FETAL FIBRONECTIN ANALYSIS

Analysis to measure the fFN concentration in a swab taken of the cervicovaginal secretions is done using the automated Rapid fFN 10Q Analyzer, Hologic. The Fetal Fibronectin Test is an *in vitro* diagnostic test that uses a single-use, disposable cassette analyzed on the automated Rapid

fFN 10Q Analyzer, to measure the fFN. The machine gives a result within 10 minutes of the swab being tested. The result is exact quantitative level of fFN and is marked as either Positive, Negative or Invalid.

People transferred from another hospital via *in utero* transfer should have an fFN swab performed if they fulfil the criteria for testing and provided they have not had an fFN swab performed at their referral hospital.
NOTE: If the person has had a digital vaginal examination in the last 24 hours at the referring hospital, the fFN test may show a false positive result and be invalid. Testing for fFN should be delayed until 24 hours after the digital vaginal examination. Transvaginal ultrasound can be used as an alternative method of predicting the risk of preterm labour, if a skilled practitioner is available.

9.1 Criteria for testing (all 3 conditions must apply):

- People with signs and symptoms of PTL between 22 and 35 weeks of gestation **(BGH variation: use up to 36 weeks of gestation to assist decision for inutero transfer)**
- Intact membranes
- Cervical dilatation < 3cm

9.2 Contraindications (do not test - test is not valid)

- Ruptured membranes
- Placenta praevia
- Placental abruption
- Moderate or gross vaginal bleeding
- Within 24 hours of sexual intercourse
- Within 24 hours after vaginal examination
- Cervical cerclage (especially within 4 weeks of cerclage placement)

All these situations can increase the false positive result (see below).

9.3 Carrying out Fetal Fibronectin Analysis
Avoid contaminating the cervicovaginal secretions with lubricants, soap, disinfectants, creams or jelly.
Use water to lubricate the speculum
Taking a fFN swab
The sample should be collected **before** digital examination is carried out. You will need:

- Sterile speculum
- Fibronectin swab
- Buffer solution
- Rapid fFN 10Q Analyzer, Hologic

  - Only use water to lubricate the sterile speculum (no cream or KY jelly)
  - Place the sterile Fibronectin swab provided in the fibronectin kits in the posterior fornix of the vagina for 10 seconds and rotate it
  - Remove swab and immerse it into the buffer solution for 10 – 15 seconds and remove it
  - Set up Rapid fFN 10Q Analyzer for the patient
  - Insert Rapid fFN Cassette into machine
  - Using a 1ml syringe pipette 200µl from the sample collected in the buffer solution into the well of the Rapid fFN Cassette
  - Complete the log book beside the machine with patient name, hospital number, date and your name
  - A result will be printed in 10 minutes

- Get 2 copies of the machine print out and place one in woman's notes and the second in the log book next to the machine beside the patient name.

9.3.1 Negative fFN result

It is reasonable to withhold tocolysis and steroids if the fFN swab is negative. Instead, the person should be observed as inpatient until the results of other investigations have been obtained.

- Analgesia should be prescribed as required.
- Inform and discuss with the person and partner, that the risk of delivering in the next 10 days is 1%.
- Educate on signs and symptoms of PTL.
- Discharge home if clinically well.
- Arrange antenatal follow up within 2 weeks with the person's consultant

For people transferred from another hospital via *in utero* transfer who do not have fFN testing available at their referring hospital and who subsequently has a negative fFN test:

- discuss the case with the on-call consultant obstetrician and consultant neonatologist
- consider transfer back to the referring hospital or discharge home depending on the clinical situation
- inform on call obstetrician from the referring hospital

9.3.2 Positive fFN result

A symptomatic person with a positive swab has an increased chance of delivering the baby preterm. Inform oncall Consultant immediately.

- offer antenatal corticosteroids as set out in section 11
- offer tocolysis in accordance to section 12
- inform NNU and neonatal sister in charge

The neonatal SpR or consultant should counsel the woman and partner appropriately.

If there is no NNU cot available then in utero transfer should be considered. Refer to Wales guidelines for in utero transfer
http://www.1000livesplus.wales.nhs.uk/sitesplus/documents/1011/All%20Wales%20In-Utero%20Guideline%20PDF.pdf.

9.4 Invalid result

An invalid result means that either too little or too much buffer solution has been added to the cassette. The analysis can be repeated using the same buffer solution and a second cassette making sure that the person running the test is familiar with the Rapid fFN 10Q Analyzer. If the test is again invalid, then transvaginal ultrasound assessment of cervical length should be used as an alternative if there is a qualified practitioner available (see below). If this is unavailable, the person should be managed according to clinical judgement. Discuss with the on call consultant.

9.5 What is the effect of digital vaginal examination and cervical cerclage on fFN results?

The presence of a cervical cerclage or performing a digital vaginal examination before Ffn testing increases the false positive rate, but does not reduce the negative predictive value of a test.

9.6 Further management

If there is evidence of ruptured membranes, follow HDUHB Guideline 645 - Preterm Labour (Spontaneous Rupture of Membranes)
If the cervix is ≥3cm dilated

- offer antenatal corticosteroids as set out in section 11

- consider tocolysis in accordance to section 12
- consider administration of magnesium sulphate for neuroprotection from 24 to ≤ 31+6 weeks

See Magnesium Sulphate for Neonatal Neuro-protection Guideline No.662

- inform NNU and neonatal sister in charge

The neonatal SpR or consultant should counsel the woman and partner appropriately.

If there is no NNU cot available then in utero transfer should be considered. Refer toWales guidelines for in utero transfer
http://www.1000livesplus.wales.nhs.uk/sitesplus/documents/1011/All%20Wales%20In-Utero%20Guideline%20PDF.pdf

10. TRANSVAGINAL ULTRASOUND ASSESSMENT OF CERVICAL LENGTH

Can be used to aid management if:

- fFN testing is contraindicated (eg digital vaginal examination done within 24 hours)
- fFN test result is invalid
- fFN test is negative but persistent uterine contractions still raise concerns that the woman is in PTL

  A transvaginal scan should only be performed by a clinician trained in transvaginal ultrasonography. People who have a cervical length at presentation of >15mm, consideration should be given to withholding steroids and to discharge from hospital.

  For a person transferred from another hospital via *in utero* transfer in whom fFN testing is contra-indicated and who subsequently has a cervical length > 15mm:
- Discuss the case with the on call obstetrician and neonatologist
- Consider transfer back to the referring hospital or discharge home depending on the clinical situation
- Inform the referring hospital on call obstetrician

11. ANTENATAL CORTICOSTEROIDS

- Antenatal corticosteroids should be offered to all people in PTL from 24+0 to 34+0 gestation in established preterm labour and in those with threatened PTL who have a positive fFN swab or a short cervix on ultrasound (≤15mm).

- If the pregnancy is less than 24 weeks of gestation, the decision for administration of maternal corticosteroids should be made after discussion with the consultant obstetrician on call and in conjunction with the neonatal team.

- From 34 to 36 weeks, there is some evidence of benefit and these cases should be discussed with the consultant obstetrician on call.

The regimen is 2 doses of betamethasone 12mg intramuscularly 24 hours apart.

The foetal half life of betamethasone is 12 hours. Accelerated courses (2 doses 12 hours apart) have not been shown to be of greater benefit and may increase side effects.

Betamethasone 12 mg given intramuscularly in two doses **or dexamethasone 6 mg given intramuscularly in four doses** are the steroids of choice to enhance lung maturation.

Evidence for other dosing regimens such as the commonly used two doses of betamethasone 12 mg given 12 hours apart is sparse (two trials, 92 women),29,30 but it would seem reasonable that as long as 24 mg of either drug is given within a 24–48-hour period, any dosing regimen can be used.

Contraindications

- Active tuberculosis

Caution

- Systemic maternal sepsis. In the presence of definite evidence of chorioamnionitis, the administration of betamethasone should first be discussed with the on call consultant and its relative merits and potential adverse effects discussed.
- In gestational diabetes or type1/2 diabetes steroids can exacerbate hyperglycaemia and the course of steroids may need to be given in conjunction with extra doses of insulin (see HDUHB guideline 632 - Management of diabetes in pregnancy).

Repeat courses of corticosteroids

If repeat courses of corticosteroids are being considered, consultant opinion must be sought. There is some evidence to support repeating corticosteroids if the first course is given very early in pregnancy. There is, however, mounting evidence that repeated courses can be harmful, associated with decreased birth weight and head size, sepsis and neonatal death.

12. TOCOLYTICS

There is no clear evidence that tocolytic drugs improve outcome and therefore it is reasonable not to use them. However, tocolysis should be considered if the few days gained would be put to good use, such as completing a course of corticosteroids or in utero transfer.

People most likely to benefit from use of a tocolytic drug are those who are in very preterm labour, those needing transfer to a hospital which can provide neonatal intensive care and those who have not yet completed a full course of corticosteroids. Tocolysis should not be used where there is a contraindication to prolonging pregnancy.

Tocolysis is indicated

- In suspected or proven preterm labour between 24^{+0} - 34^{+0} weeks gestation.
- If the cervix is < 4 cm dilated
- With intact membranes
- Or for transfer to neighbouring unit irrespective of gestational age and state of membranes.

Consider tocolysis in other circumstances only after discussion with a consultant.

Relative Contra-indications for Tocolysis

- Ruptured membranes (unless reviewed by consultants)
- Fetal distress
- Intrauterine infection
- Antepartum haemorrhage
- Any maternal medical condition that warrants delivery (e.g. pre-eclampsia)
- Any maternal medical disorder where chosen tocolytic drug is contra indicated, see below.

Only four drugs are licensed in the UK for tocolysis (ritodrine, salbutamol, terbutaline and atosiban). Ritodrine & salbutamol **should no longer be used because of the maternal side effects** [7-9].

Nifedipine and Atosiban have comparable effectiveness in delaying birth for up to seven days. Compared with beta-agonists, Nifedipine is associated with improvement in neonatal outcome, although there are no long-term data.

If **Atosiban** is requested by receiving unit refer to Appendix 1 – but note HDUHB does not stock Atosiban routinely.

Nifedipine

The suggested dose of Nifedipine is 20mg TDS (an initial oral 20mg dose followed by 20mg three times daily).

Nifedipine is contraindicated if the person has cardiac disease and should be used with caution if she/he has diabetes or multiple pregnancy, owing to the risk of pulmonary oedema.

1. Observations:
   BP every 15 minutes for first 2 hours after 1st dose and
   then 4 hourly

2. Commence CTG for fetal well-being unless inutero transfer in progress

3. **Nifedipine rarely causes a drop in BP in normotensive women**

Specific contraindications to Nifedipine

- Hypovolaemia
- Porphyria
- Cardiogenic shock
- Advanced aortic stenosis
- Within 1 month on myocardial infarction
- Unstable or acute attack of angina
- Treatment with magnesium

13. KEY NOTES

- Remember the diagnosis of labour is difficult
- Consider underlying causes
- Use betamethasone early
- Use tocolysis cautiously
- Consider antibiotics if ruptured membranes
- Liaise with neonatologists
- Do no transfer if risk of imminent delivery

14. MONITORING

A regular audit will be carried out considering the following standards:

1. Number of women fFN positive who deliver in the next 7 days
2. Number of women fFN negative who deliver in the next 7 days
3. Number of women with cervical length ≤ 15mm on transvaginal ultrasound who deliver in the next 7 days
4. Number of women with cervical length > 15mm on transvaginal ultrasound who deliver in the next 7 days
5. Number of *in utero* transfers with fFN negative and do not deliver in the next 7 days
6. Number of *in utero* transfers with cervical length > 15mm on transvaginal ultrasound and do not deliver in the next 7 days
7. Number of women who received a tocolytic drug for suspected prteterm birth
8. Choice and duration of tocolytic drug
9. Proportion of women on local first-line tocolytic drug and on multiple drugs
10. Number of women receiving a course of antenatal corticosteroids
11. Births before 34 weeks of gestation
12. Proportion of women and babies with adverse effects associated with tocolyic drugs
13. Number of babies born without exposure to antenatal corticosteroids
14. Use of a guideline on tocolysis

Refer to Appendix 5 - Audit Proforma on Predictive Value of fFN & Cervical Length
Audit results will be considered by the Women and Children's Quality, Safety and Experience Group.

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16. APPENDIX 1 - ATOSIBAN (TRACTOCILE)

Suggested dose: an initial bolus of 6.75mg over one minute, followed by an infusion of 18mg/hour for 3 hours, then 6mg/hour for up to 45 hours (to a maximum of 330mg).

Atosiban

- Is an Oxytocin antagonist
- Requires IV administration
- Initial bolus, then high dose infusion for 3 hours, followed by low dose infusion for up to 45 hours
- Reassess after 18 hours of treatment
- Has a half-life of 13 minutes therefore no additional risk of PPH
- Re-treatment is an option.

Method of administration

Atosiban (Tractotile) is administered IV in three stages:

1) Loading dose – slow bolus injection over one minute of 6.75mg Atosiban (0.9 ml of 7.5mg/ml solution for injection
2) Initial infusion – high dose of 300ug/min Atosiban for 3 hours only.
   Preparation: withdraw (and discard) 10mls of a 100ml NSaline infusion. Add 10mls of Atosiban 7.5mg/ml concentration (two ampoules of 5mls each). Set infusion speed to 24mls/hr (this will use 72mls in 3 hours – the rest may be used for step 3).
3) Maintenance infusion – low dose infusion of 100ug/min Atosiban for up to 45 hours; stop earlier once contractions have settled for 4 hours. Most patients are expected to settle in 13 hours.
   Preparation: repeat as for step 2. Reduce infusion rate to **8mls/hour**.

Specific contraindications for Atosiban

Known hypersensitivity to Atosiban or any of the contents in Tractocile®

17. APPENDIX 2 - SCREENING FOR PRETERM LABOUR IN THE ANTENATAL BOOKING CLINIC – FLOW CHART

Screening for preterm labour in the antenatal booking clinic – flow chart

Worldwide there are 15 million preterm births that take place per annum. One million of these preterm babies dies. In the UK this has an estimated cost of £2.9 billion per annum.

Preterm birth is one syndrome with many causes. These are namely Cervical disease, Decline in progesterone action, Uterine overdistension, Decidua senescence, Vascular disorder, Infection, Stress, and Breakdown of maternal-fetal tolerance.

Risk factors for preterm birth where screening is advised (National audit – Preterm Network, UK):

1. Previous preterm birth
2. Previous Preterm Prelabour Rupture of Membranes (PPROM)
3. Recurrent 2nd trimester loss
4. 2 X Large Loop Excision of the Transformation Zone (LLETZ)
5. Cone biopsy
6. Uterine anomalies

CERVICAL LENGTH AT 16/40. IF NOT PERFORMED AT 16/40, CONSIDER DOING BETWEEN 16/40 AND 22/40 (SHOULD BE DONE BY TVS)

NICE.org.uk

IF CERVICAL LENGTH > 25 MM WITH RISK FACTORS 4, 5 and 6 CAN BE FOLLOWED UP BY THEIR CMW

National Preterm Birth Group

IF CERVICAL LENGTH IS <25 MM, PATIENT MUST BE OFFERED EITHER VAGINAL PROGESTERONE OR CERVICAL CERCLAGE
NICE.org.uk

IF CERVICAL LENGTH > 25 MM WITH RISK FACTORS 1, 2 AND 3

INDIVIDUALISED MANAGEMENT PLAN NEEDED*
National Preterm Birth Group

CERVICAL LENGTH <25 MM AND PREVIOUS TREATMENT WITH EITHER PROGESTERONE OR CERVICAL CERCLAGE

SERIAL CERVICAL LENGTH AND fFN TEST / Actim partus NEEDED

CERVICAL LENGTH >25 MM AND WITH RISK FACTORS 1, 2 AND 3 MAY NEED SERIAL CERVICAL LENGTH AND fFN /Actim partus *

For cervical cerclage monofilament sutures are recommended **ETHILON W748 OR W738**
CYCLOGEST 200 mg pessary once daily is recommended as progesterone therapy.
*Screening to be done every two weeks with cervical length and fFN until she crosses her risk line.

18. APPENDIX 3 - GUIDANCE FOR ANTENATAL CORTICOSTEROID ADMINISTRATION

Antenatal corticosteroid administration significantly reduces the risk to the neonate of respiratory syndrome, intraventricular haemorrhage, and death. The advised dosage is either Betamethasone 12mg IM (two doses 24hrs apart) or Dexamethasone 6mg IM (four doses 12hrs apart).
Repeat courses of antenatal corticosteroids are not recommended.

Optimum benefit is obtained within seven days of administration of corticosteroids.

The benefits and risks of antenatal corticosteroid administration should be discussed with the patient prior to administration.

Patient information (RCOG) to be given:
https://www.rcog.org.uk/globalassets/documents/patients/patient-information-leaflets/pregnancy/pi-corticosteroids-in-pregnancy.pdf

Indications for administering antenatal corticosteroids:

1. Preterm Prelabour Rupture of Membranes (PPROM)
2. Antepartum Haemorrhage (APH)
3. Elective preterm delivery for maternal or fetal indications.
4. Pre term labour – use fFN and cervical length measurement for risk assessment (QUiPP application can be used – not validated but recommended by UK Preterm Clinical Network)
5. Elective caesarean section less than 39 weeks of gestation

GESTATIONAL AGE	RECOMMONDATION
Between 23+0 and 23+6	No proven benefit. Need consultant obstetrician and consultant neonatologist involvement. Informed decision is required.
Between 24+0 and 25+6 gestation	Consider antenatal corticosteroids
Between 26+0 and 33+6	Offer antenatal corticosteroids
Between34+0 and 35+6	Offer antenatal corticosteroids (2017)
Elective caesarean section less than 39 weeks	Offer antenatal corticosteroids
TYPE 1, TYPE 2 AND GESTATIONAL DIABETES	
Induction of labour (IOL) - Type 1 diabetes, Type 2 diabetes and gestational diabetes – steroids required if you consider IOL before 37/40.	
Elective caesarean section (elLSCS) - Type 1 diabetes and Type 2 diabetes – if elLSCS is planned before 39/40 steroids are required.	
Do not wait to administer further doses of steroids if following the initial dose of steroids delivery of the baby is indicated for maternal or fetal reasons. Consider immediate delivery.	
WHERE ANTENATAL STEROIDS ARE NOT INDICATED	
Gestational diabetics undergoing IOL at/after 37 weeks of gestation	
Failed IOL undergoing caesarean section at/ less than 37 weeks of gestation	
CONTRAINDICATION FOR STEROIDS	
Chorioamnionitis	Maternal sepsis

REFERENCES

- National Institute for Health and Care Excellence. Preterm labour and birth. NICE guideline No 25. 2015.
- World Health Organization. WHO recommendations on interventions to improve preterm birth outcomes. 2015.
- http://dx.doi.org/10.1001/jamapediatrics.2017.0602
- http://dx.doi.org/10.1056/NEJMoa1516783
- http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD004454.pub3/full

19. APPENDIX 4 - ST THOMAS' HOSPITAL PROTOCOL FOR SYMPTOMATIC PATIENTS (MODIFIED)

The Rapid 10Q fFN machines, which also give a quantitative result, can aid better risk discrimination (Abbott et al, 2012). The table below indicates risk of delivery according to quantitative fFN value, along with management guidelines:

fFN value	% who will deliver within 2 weeks	% who will deliver at <34 weeks	Management guidelines Valid for 24+0 (or earlier where the fetus is potentially viable) to 34+6 weeks
0-9	<2	<2	Discharge with routine midwife follow up
10-49	<2	5-15	Discharge with routine consultant follow up
50-199	5-15	10-15	• Admit • Give betamethasone 12mg 24 hours apart
200-499	30	30	• Admit • Give betamethasone 12mg 24 hours apart • Tocolysis with Nifedipine 20mg stat then 20mg TDS
>500	50	75	• Admit • Give betamethasone 12mg 24 hours apart • Tocolysis with Nifedipine 20mg stat then 20mg TDS

Important point
False positive may occur as a result of blood or semen, therefore history of sexual intercourse in last 48 hours and PVB should be obtained.

20. APPENDIX 5 - Audit Proforma on Predictive Value of fFN & Cervical Length

1) BMI:
2) Gravida: Para:
3) Previous delivery ≤ 37/40 Y / N
4) Obstetric history (incl. TOP/miscarriage, late miscarriage, stillbirth):
5) Year: Mode of Del.: Gestation: Problems:
6) Procedures on Cx - LLETZ etc. Y / N
7) Any problems in this pregnancy:
8) Gestation at presentation (accurate):
9) First episode: Y / N Repeated admission: Y / N
10) Symptoms: PPROM: Y / N APH: Y / N Contractions: Y / N
11) Comments:
12) From home: Referred by midwife: Transferred from other hospital:
13) If from another hospital:
    fFN done Y / N Results: Neg / Pos
    VE Cx Tocolytics Y / N Steroids Y / N
14) Comments:
15) Findings on admission:
    Contractions: Y / N Present on CTG: Y / N
    Cx
    Membranes Intact / SROM Amniquick Pos / Neg/ not done

CRITERIA

1) 22-35 wks with s/s of PT labour
2) Membranes intact
3) Cervical dilatation <3cm

Contraindications (do not test- test is not valid)

- Ruptured membranes
- Placenta previa / abruption
- Moderate or gross vaginal bleeding
- Within 24 hours of sexual intercourse
- Within 24 hours after vaginal examination
- Cervical cerclage (especially within 4 weeks of cerclage placement)

16) Criteria for fFN met: Y / N
17) fFN offered /explained: Y / N
18) fFN done by: mw / SHO / SpR
19) Result: Pos / Neg / Invalid
20) fFN value: ng/ml
21) Comments:
22) Ultrasound - Cervicometry: Y / N
23) TVS / TAS
24) USS by: Mid grade / Cons
25) Cervical length: mm
26) Funnelling: Y / N
27) Further management decided by whom: SHO / Mid grade / Cons
28) Steroids given: Y / N Tocolytics: Y / N Regime:
29) Patient admitted: Y / N
30) Date of discharge:
31) Transfer in-utero: Y / N Where:
32) If patient treated/admitted/transferred when fFN neg and/or Cx ≥15mm:
    Reasons: Decided by:
33) Gestation at delivery: Reasons for delivery: