Fetal Fibronectin

Guideline for Use in the Management of Preterm Labour

Practice Guideline

Adapted with Revisions Approved by Ontario's
Provincial Maternal-Newborn Advisory Committee (December, 2008)

***Note*: Original Guideline produced by a sub-committee of the Canadian Perinatal Partnerships Coalition, October 15, 2007 with adaptations from the Child Health Network for the Greater Toronto Area (CHN) and the British Columbia Reproductive Care Program (BCRCP).**

Ontario

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1. Background

A large percentage of the membership of the Canadian Perinatal Partnerships Coalition (CPPC) has reported working on a process to implement a fetal fibronectin (fFN) program in their region. To maximize resources and minimize duplication, we decided to work together and produce the documents, procedures, and monitoring/audit tools needed to implement a fFN program. The intent is that the resources produced are applicable to any practice area in the country. This document was adapted from guidelines already in use by the British Columbia Reproductive Care Program (BCRCP) and the Child Health Network for the Greater Toronto Area (CHN). Their original documents were developed by expert panels in their regions and were widely distributed for comment and input.

The value of using fFN testing is in the potential to avert maternal transfers from regional and community hospitals and optimize the use of tertiary antenatal and neonatal beds. It is also expected that admissions to both community and regional hospitals could be reduced as physicians could be assured that mothers with a negative fFN test would not deliver their babies within 14 days.

2. Disclaimer

The CPPC have no affiliation with Hologic LP the sole provider of the Fetal Fibronectin Test and will not receive any benefit from Hologic LP related to the development of this guideline.

This guideline is intended for use only by professional perinatal health care providers. The information it provides is not suitable for a non-professional audience and is not intended as medical advice. The guideline has been developed in Canada for use by professionals in Canada only. The content of this guideline is not intended to dictate exclusive courses of practice.

While attention has been given to ensure that this procedure reflects available research and expert consensus, CPPC does not guarantee that the information it contains is accurate, complete or up-to-date. CPPC is not responsible for any errors or omissions or injury, loss, damage, cost or expense arising from, or as a result of, reliance on this information.

3. Introduction

3.1. Preterm Labour

Preterm birth is the major cause of neonatal morbidity and mortality in reproductive care. The rate of preterm birth has been rising in Canada from 6.6% of live births in 1991 to 7.6%of live births in 2000 (Canadian Perinatal Health Report, 2003). In Ontario the preterm birth rate is 8.5% (OPSS Report, 2008). There are a number of reasons for this increase including higher rates of multiple gestation, advancing maternal age and better fetal surveillance identifying babies who would benefit form elective preterm delivery.

3.2. Fetal Fibronectin

Fetal Fibronectin (fFN) is a glycoprotein produced by the chorionic membranes and is localized to the deciduas basalis adjacent to the intervillous space. Its primary purpose appears to be that of an adhesion molecule (tissue glue) which helps bind the chorionic membranes to the underlying maternal decidua.

It is normally found in cervico-vaginal secretions until 22 weeks gestation but is virtually never found between 24 and 34 weeks gestation unless the cervix has undergone premature effacement and dilatation, usually in association with symptomatic uterine contractions. It can also be released in response to inflammation or separation of amniotic

membranes from the deciduas. There is a strong association between the presence of Fetal Fibronectin in cervico-vaginal secretions and preterm labour after 24 weeks gestation.

Use of the fFN test will assist clinicians to determine which women require transfer to level 2 or tertiary centres, decrease unnecessary admissions and make better use of scarce tertiary maternal and NICU beds.

3.3. Literature Review

An overview of the literature on fFN testing and clinical outcomes is available in Appendix A. In summary, trials have shown an association between the presence of fFN and preterm birth as well as a decrease in the risk of preterm birth when tests are negative for the presence of fFN. A negative test confers a more than 95% likelihood of the woman remaining undelivered for the 14 days.

3.4. Purpose of the Fetal Fibronectin Test

The purpose of testing for Fetal Fibronectin in women with symptoms of premature labour is to:

1. Prevent/decrease unnecessary admissions to community, regional and tertiary hospitals thereby improving access for those women who most require services.
2. Prevent/decrease unnecessary transfers of mothers with symptoms of preterm labour to tertiary or regional centres
3. Decrease the number of out-of-region transfers
4. Decrease cost associated with an admission to a tertiary (or community and regional hospital) - especially those related to a stay in the birthing unit.
5. Improve identification of women who require corticosteroid and tocolytic therapy
6. Provide reassurance to mothers and their families that birth of their baby prematurely is highly unlikely within fourteen days of the onset of symptoms when the test is negative.
7. Reduce stress and anxiety for the woman and her family due to reassurance and absence of unnecessary transfer out of her home community

3.5. Cost

The cost of processing each fFN test is approximately $125 plus minimal costs associated with laboratory equipment and upkeep. The use of the test according to these guidelines will ensure appropriate resource use across our perinatal system.

4. General Recommendations:

1. All women presenting in the Emergency Department or Birthing Unit with one or more signs/symptoms of threatened preterm labour (Figure 1) should be assessed quickly and fFN testing performed if they meet the criteria.

Figure 1 Signs of Threatened Preterm Labour

Regular uterine contractions >6 per hour Pelvic pressure Low abdominal pain and/or cramps Low backache

NOTE: PRIOR TO ANY VAGINAL EXAMINATION, A SPECULUM EXAM SHOULD BE DONE AND THE SWAB FOR FETAL FIBRONECTIN OBTAINED. THE DECISION TO SEND THE SWAB FOR TESTING CAN BE MADE ONCE THE PATIENT's PHYSICAL ASSESSMENT IS COMPLETE.

2. **Indications for Processing the Swab**
    - Intended admission/transfer of women between 24 and 34 completed weeks
        i. Threatened preterm labour (Figure 1)
        ii. Intact amniotic membranes
        iii. Cervix <3 cm dilatation
        iv. Established fetal well-being
    - Intended administration of antenatal corticosteroids

3. **Contraindications for Processing the Swab**
    - Estimated gestational age (EGA) <24 weeks or >34 completed weeks
    - Preterm rupture of membranes (PROM)
    - Cervix ≥3 cm dilatation
    - Cervical cerclage
    - Active vaginal bleeding
    - Vaginal exam or sexual intercourse in the past 24 hours

4. **Specimen Collection**
    - Use only the Hologic LP Fetal Fibronectin Kit
        i. Equipment required includes the swab, collection tube, tube cap, test cartridge and instrument based system to perform the fFN test.
    - Collect specimen via a speculum exam using an unlubricated speculum with specific fFN swab (See Appendix B).
    - Speculum exam must occur before vaginal ultrasound, before digital examination and without the use of lubricants (all can alter predictability of the test).
    - If any of the above exams have taken place, wait 24 hours and then obtain the test.
    - If a swab cannot be processed within 8 hours of collection, refrigerate specimen until processing is performed.
    - Process the swab within 3 days of specimen collection.

NOTE: Once the swab has been obtained, if subsequent physical exam does not indicate that there are sufficient signs of preterm labour (or if other contraindications are present i.e., ruptured membranes, cervical dilatation > 3 cm, etc.), the swab should be discarded and the test NOT performed.

5. **Test Results**
    - Positive ≥ 50 ng/ml to confirm values or +ve / -ve
    - Negative < 50 ng/ml

    The test result is reported as a qualitative positive or negative value rather that a quantitative value.

6. **Factors Affecting Accuracy of the Test**
    - False positive tests may be caused by:
        i. Digital exam prior to the speculum collection of the sample
        ii. More than a minimal amount of blood in the specimen (fFN is present in plasma)
        iii. The presence of amniotic fluid in the specimen (amniotic fluid contains high levels of fFN)
        iv. Intercourse within the previous 24 hours (fFN is present in seminal fluid)
        v. Feminine hygiene products (douching)
    - False negative tests may be caused by:
        i. Presence of a lubricant on the speculum

7. **Negative Test Result**
    - Indicates that delivery is not likely to take place within 7-14 days (>95% accuracy)
    - Consider:
        - Discharge patient from hospital with instructions to return if symptoms worsen. She should limit activities that aggravate her symptoms. Ultimately, patient disposition may be dependent on geographical, weather and/or other medical circumstances.
        - Follow up care may include a vaginal ultrasound to assess cervical length (If cervical length is >2.5 cm it provides further reassurance that delivery will not occur preterm) +/- a swab for bacterial vaginosis.
        - Re-assessment should be done within 7-14 days with ongoing education regarding the signs and symptoms of preterm labour. (repeat the swab only as indicated through clinical re-assessment). *An exception to the time for reassessment may be made if the woman lives in a remote community and fly out transportation must be arranged. In such a case the clinician may repeat the swab testing if the woman is symptomatic. Decisions regarding her disposition ultimately should be discussed with the mother, the remote health care providers and the consulting obstetrical service providers.*

8. **Positive Test Result**
    - Indicates a higher risk of preterm delivery quoted by the vendor to be in the arena of 16-17%.
    - Consider:
        i. Admission or transfer of the woman to an appropriate facility for treatment of preterm labour and possible delivery of a preterm baby
            1. <32 weeks – Tertiary centre
            2. ≥32 weeks – Level 2 or Level 2+ centre
        ii. Administration of tocolytics and/or corticosteroids as indicated

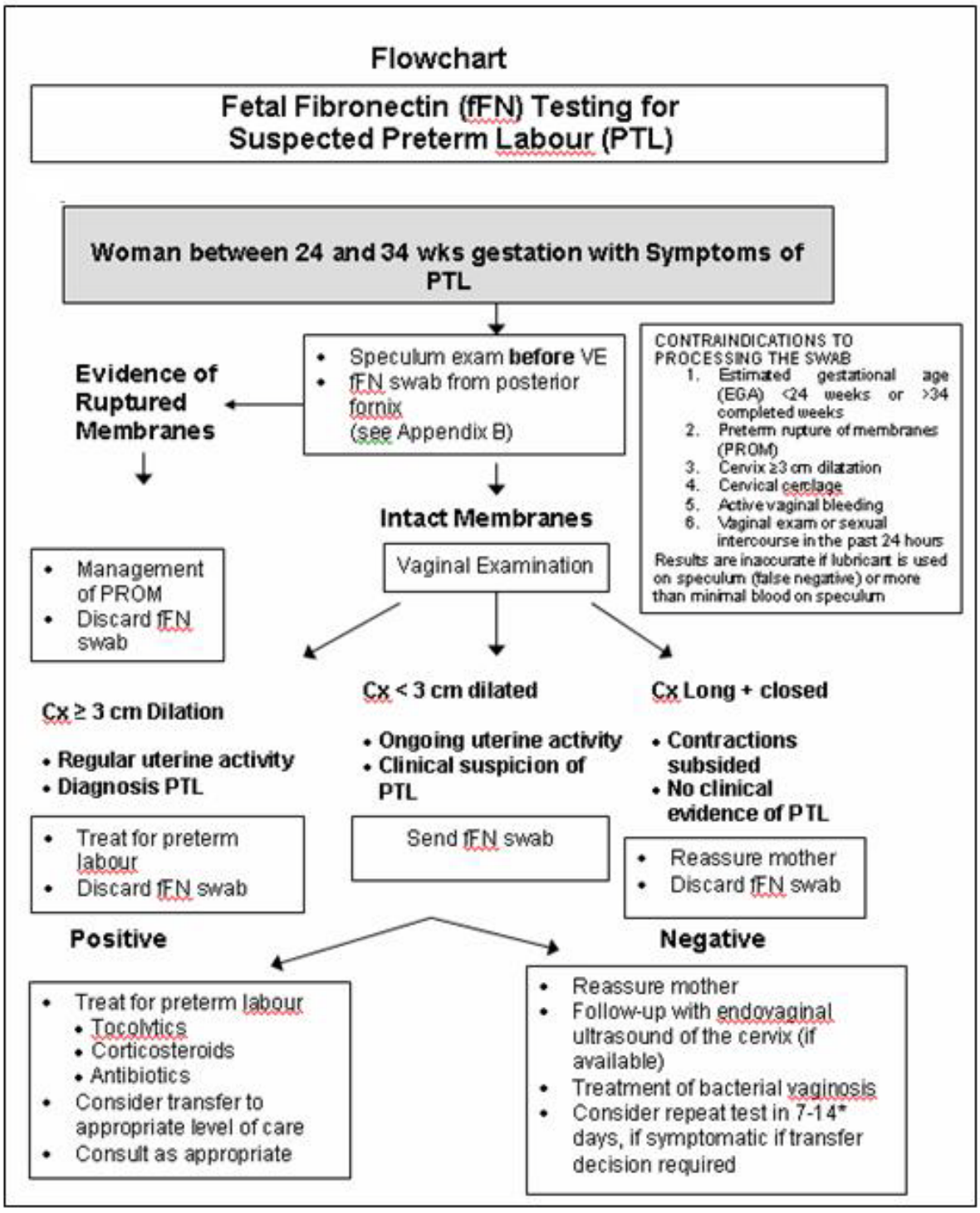
9. **Patient Education**
    - The purpose and function of the test should be explained to each woman in order to avoid ‘patient demand” for the test in subsequent weeks

10. **Inappropriate Use of the Test**
    - fFN testing is NOT meant to be used in the absence of symptoms of PTL as a means of reassurance that PTL will NOT occur.

5. Evaluation/Audit

An audit tool monitoring the following parameters will be submitted with requests for test kit reimbursement to Ontario Perinatal Surveillance System for a regular review of the use and reliability of the test as well as the impact on the regional system of perinatal care. The following indicators will be monitored:

1. The number of fFN tests performed by organization
2. The number of negative/positive tests recorded
3. Patient disposition (home, admitted, transferred by air, ground or combination to another centre)


Flowchart
Fetal Fibronectin (fFN) Testing for Suspected Preterm Labour (PTL)
Woman between 24 and 34 wks gestation with Symptoms of PTL
Speculum exam before VE
fFN swab from posterior fornix (see Appendix B)
Evidence of Ruptured Membranes
Intact Membranes
CONTRAINDICATIONS TO PROCESSING THE SWAB
1. Estimated gestational age (EGA) <24 weeks or >34 completed weeks
2. Preterm rupture of membranes (PROM)
3. Cervix ≥3 cm dilatation
4. Cervical cerclage
5. Active vaginal bleeding
6. Vaginal exam or sexual intercourse in the past 24 hours
Results are inaccurate if lubricant is used on speculum (false negative) or more than minimal blood on speculum
Management of PROM
Discard fFN swab
Vaginal Examination
Cx ≥ 3 cm Dilation
Regular uterine activity
Diagnosis PTL
Cx < 3 cm dilated
Ongoing uterine activity
Clinical suspicion of PTL
Cx Long + closed
Contractions subsided
No clinical evidence of PTL
Treat for preterm labour
Discard fFN swab
Send fFN swab
Reassure mother
Discard fFN swab
Positive
Negative
Treat for preterm labour
Tocolytics
Corticosteroids
Antibiotics
Consider transfer to appropriate level of care
Consult as appropriate
Reassure mother
Follow-up with endovaginal ultrasound of the cervix (if available)
Treatment of bacterial vaginosis
Consider repeat test in 7-14* days, if symptomatic if transfer decision required

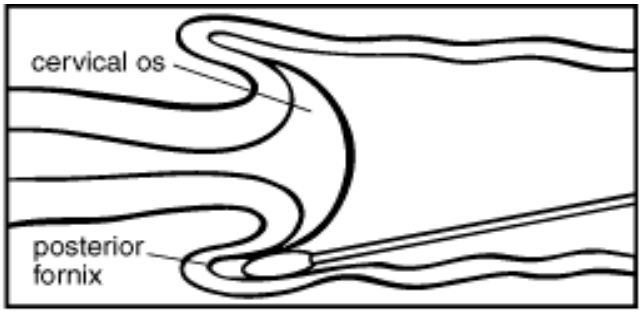
Guideline APPENDIX A

3 Easy Steps to Collect the fFN Swab

The fFN specimen should only be collected using the Hologic LP fFN Kit. The kits and testing device are only available through:

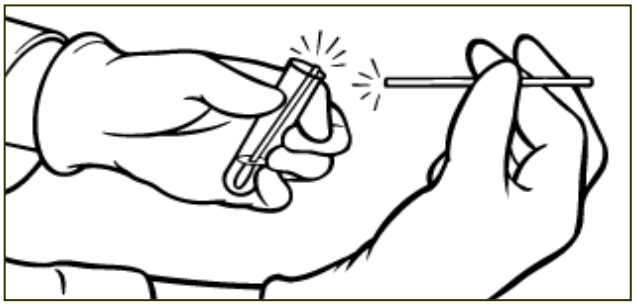
1

During speculum examination, lightly rotate the swab across the posterior fornix of the vagina for 10 seconds to absorb cervicovaginal secretions.



2

Remove swab and immerse tip in buffer. Break the shaft at the score even with the top of the tube.



3

Align the shaft with the hole inside the tube cap and push down tightly over the shaft, sealing the tube. Ensure the shaft is aligned to avoid leakage.