

Fetal Fibronectin

Guideline for Use in the Management of Preterm Labour

Practice Guideline

(Insert own Logo Here)

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**Produced by a sub-committee of the Canadian Perinatal Partnerships Coalition
Adapted from the Greater Toronto Area Child Health Network (CHN) and the
British Columbia Reproductive Care Program (BCRCP)**

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 Greater Toronto Area Child Health Network (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.

Disclaimer

The CPPC have no affiliation with Adeza, the sole provider of the Fetal Fibronectin Test and will not receive any benefit from Adeza 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.

Introduction

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 (insert name of region here) the PTB rate is (insert your local data here) (see Figure 1). 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 from elective preterm delivery. (If any regional data on this is available – it can be inserted here and labelled as Figures 2-?)

Because the diagnosis of preterm labour based on clinical suspicion, examination and contraction history is relatively inaccurate, clinicians could benefit from a test that will help them improve the accuracy of diagnosis.

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.

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.

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
2. Prevent/decrease unnecessary transfers of mothers with symptoms of preterm labour to tertiary or regional centres
3. Decrease the numbers of out-of-region transfers
4. Decrease costs 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

Cost

The cost of processing this test is about \$100 per test plus the costs associated with laboratory equipment and upkeep. Clinicians are encouraged to be judicious in the use of fFN testing.

General Recommendations:

1. All women presenting in the Emergency Department or Birthing Unit of with one or more signs/symptoms of threatened preterm labour (Figure 1) should be assessed quickly. (If a mandatory consult is required, insert the sentence here or else insert a statement that they may want to speak with the obstetrician/consultant in the referral centre to discuss management options) 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 PHYSICAL ASSESSMENT IS COMPLETE.

2. Indications for Testing

- 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 Testing

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

4. Specimen Collection

- Use only the Adeza™ 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 test cannot be performed within 8 hours of collection, refrigerate specimen until test is performed
- Perform test 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 \geq 50 ng/ml
- Negative < 50 ng/ml

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)
- False negative tests may be caused by:
 - i. Presence of a lubricant on the speculum

7. Positive Test Result

- Indicates a higher risk of preterm delivery
- 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

8. Negative Test Result

- Indicates that delivery is not likely to take place within 7-14 days (>95% accuracy)
- Discharge home with instructions to return if symptoms worsen. She should limit activities that aggravate her symptoms. This advice is dependent on geographical, weather and 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-evaluate in 7-14 days

9. Patient Education

- The purpose and function of the test should be explained to each woman in order to decrease ‘patient demand’ for the test in subsequent weeks

10. Inappropriate Use of the Test

- This test should only be used as an adjunct to the clinical suspicion of preterm labour. It is **not** meant to be used when no symptoms are present as a reassurance that PTL is not likely to occur in coming weeks.

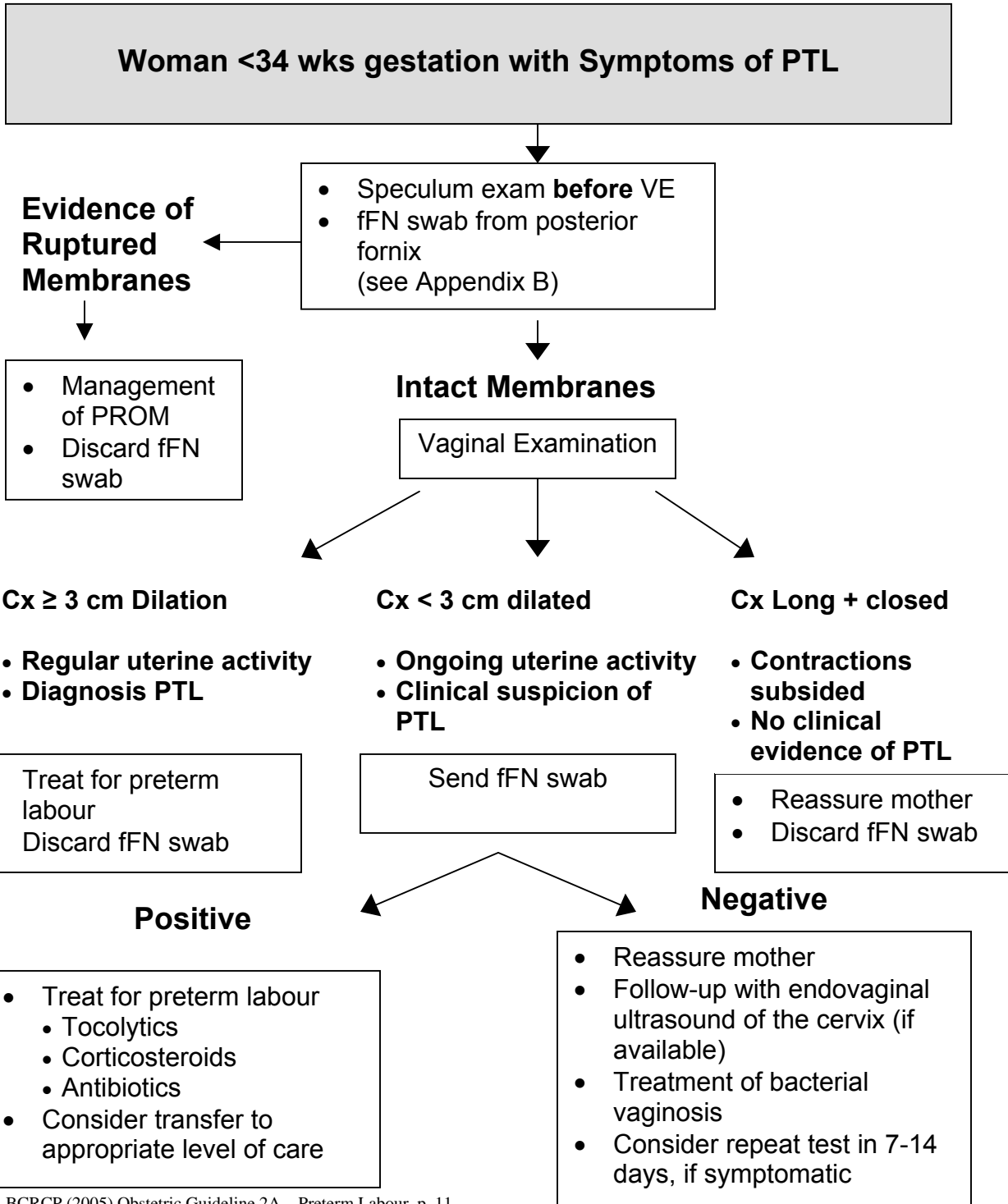
Evaluation/Audit

An audit tool monitoring the following parameters will be submitted to **insert appropriate name here** 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. The number of transfers of women who have had fFN testing to other hospitals for the diagnosis of premature labour
4. The number of transfers avoided through negative test results
5. Estimated cost of the test to the system (# of tests performed multiplied by the cost of the test)
6. Estimated savings to the system days avoided by use of test
7. Patient days for admission for preterm labour and compare to retrospective patient days in previous year prior to implementation of the fFN test

Flowchart

Fetal Fibronectin (fFN) Testing for Suspected Preterm Labour (PTL)



Appendix A

Literature Review (prepared by Dr. Graeme Smith - Kingston General Hospital, and adapted from the Nova Scotia Reproductive Care Program)

A large and compelling body of literature confirms the value of fFN testing to determine the risk of preterm birth in women with symptoms of preterm labour. A review of 40 studies involving over 11,000 pregnant women demonstrated that symptomatic women with a negative fFN test had a very low probability (<2%) of delivery within 7-14 days, whereas 20-30% of fFN positive women deliver within 14 days of testing.¹ In the largest study published to date, Peaceman, et al., evaluated the predictive accuracy of fFN in a multicentre trial of 763 women presenting with symptoms of preterm labour.² Only 1 in 25 (4%) of symptomatic women in the study delivered preterm. Fetal fibronectin was positive in 20% of the study population and negative in 80%. One in six (17%) women with a positive fFN result delivered within 14 days, whereas only 1 in 125 (<1%) of women with a negative fetal fibronectin test delivered within 14 days. Based on available evidence, fFN testing has been shown to be useful in women with symptoms of preterm labour to identify those with negative values and a reduced risk of preterm birth, thereby avoiding unnecessary interventions. On the other hand, the small percentage of symptomatic women who have a positive fetal fibronectin and are at increased risk of preterm birth are more likely to receive appropriate transfer and/or admission to a tertiary perinatal care center.

The largest Canadian data comes from The Fetal Fibronectin Testing for Suspected Preterm Labour Study which was conducted at the IWK Health Center and five regional health centers in Nova Scotia from April 2003 to March 2004. Women who presented to these six centers during the twelve-month study period with suspected preterm labour between 24 and 30 weeks gestation, who had intact membranes and cervical dilatation less than 3 cm, were invited to participate. Of the 395 study participants with fFN results and pregnancy outcome information, 30 (8%) had a positive fetal fibronectin test result and 365 (92%) had a negative test result. For all of the women with suspected preterm labour who participated in this study, only 1 in 30 (3%) actually went on to deliver within the next two weeks. For those women who had a positive fFN result, 1 in 4 (25%) delivered within two weeks, whereas only 1% of women with a negative fFN result delivered within 14 days. More detailed analysis of the diagnostic accuracy of fFN testing for delivery ≤ 7 days, ≤ 14 days, < 34 weeks and < 37 weeks confirmed the same high level of reliability and test performance of fFN testing in Nova Scotia as demonstrated elsewhere. The study results also demonstrated that fFN testing was superior to clinical parameters in accurately identifying women who are truly at risk or not at risk for preterm birth. In terms of impact on obstetric practice, only 12% of women with a negative fFN result presenting to the IWK Health Center were admitted and less than 4% of fFN negative women were transferred from the regional centers to the IWK for admission and further assessment. Total births, perinatal deaths and preterm birth rates during the twelve-month baseline period before the study and during the study period were similar suggesting that the implementation of fFN testing did not result in an increase in preterm births occurring in the regional centers.

A growing number of studies have demonstrated that implementation of fFN testing has resulted in significantly reduced preterm labour admissions, maternal transfers, length of stay, and use of tocolytic agents.²⁻⁵ These reductions in utilization of health care resources have translated to significant cost savings in tertiary care and regional health centers in the United States and Canada. The impact of fetal fibronectin testing for suspected preterm labour on hospital admission rates and health care costs in Nova Scotia and British Columbia is currently being evaluated. Preliminary data suggest significant reduction in reproductive health care utilization and costs during the study period compared to the twelve-month baseline period prior to fFN implementation.

Although system-wide health care costs will be reduced by implementing fFN testing there may be small increases to the Laboratory costs. Clinicians may choose to admit women with symptoms of preterm labour for a short period of observation, even if they have had a negative fFN test, particularly those who live a distance from a health care facility. Such admissions reflect concern for patient well being rather than lack of confidence in the test result. In the facilities where fFN testing is being introduced (i.e. those that did not participate in the

pilot), these admissions may also be related to concerns for patient safety. Over the course of the pilot project in Nova Scotia, these precautionary admissions decreased noticeably. As noted above, all admissions for preterm labour will be reported so that any increases in regional facilities can be reviewed.

In summary, available evidence from the literature and from a recent study in Nova Scotia have clearly demonstrated that the rapid fetal fibronectin test for evaluation of women with suspected preterm labour is a reliable predictor of preterm birth and results in a reduction in preterm labour admissions, maternal transfer rates, length of stay, and reproductive health care utilization and costs without compromising neonatal outcome for women at risk for preterm birth. In addition to these benefits, health care providers can avoid unnecessary interventions with confidence and allow the majority of women with suspected preterm labour to remain at home with their families in their own communities.

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Further Reading

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APPENDIX B

3 Easy Steps to Collect the fFN Swab

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

***** ADEZA Customer Service at 1- 888 -567-3817 *****

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.

