MATERNAL911®






Preterm Labor

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Course Description:

When neonates enter the world prematurely, it is a long road to recovery. Preterm labor is certainly a factor for prematurity at birth. The Maternal 911 Preterm Labor course will help participants review and gain knowledge. This will help to prevent and resolve preterm labor and thus birth. The goal is a term birth allowing better success for the newborn. The recognition and management of preterm labor may have a huge impact in this arena of prematurity.

Approximate Time to Complete: 40 minutes

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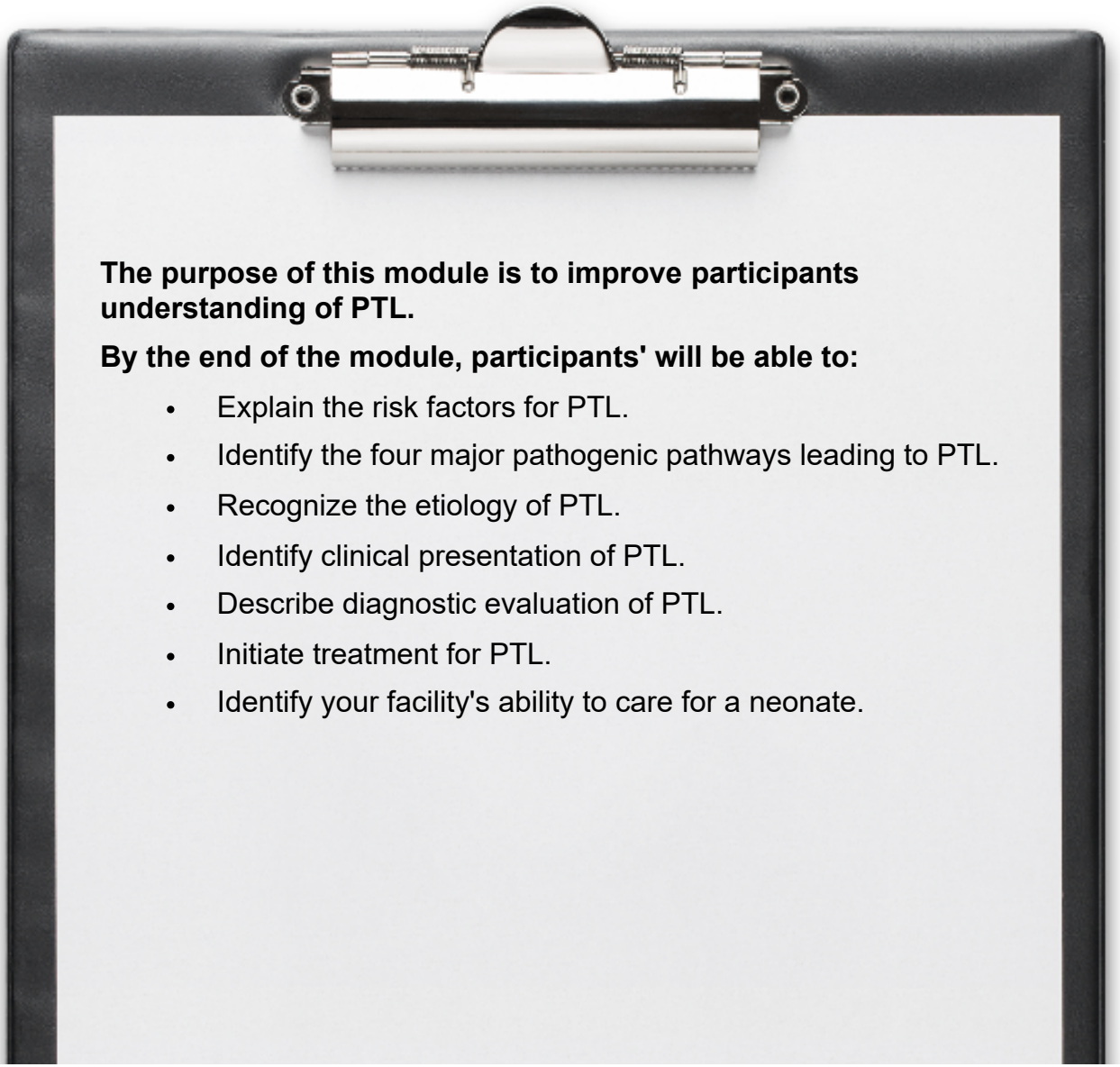

The purpose of this module is to improve participants understanding of PTL.

By the end of the module, participants' will be able to:

- Explain the risk factors for PTL.
- Identify the four major pathogenic pathways leading to PTL.
- Recognize the etiology of PTL.
- Identify clinical presentation of PTL.
- Describe diagnostic evaluation of PTL.
- Initiate treatment for PTL.
- Identify your facility's ability to care for a neonate.

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Preterm labor likely results from:

This obstetric complication is caused by local changes that prematurely stimulate the uterus to contract or by premature withdrawal of suppressive factors that are designed to maintain uterine quiescence [26].

A woman's likelihood of preterm delivery is determined by multiple genetic, environmental and immunological factors.

- However, the biggest risk factor for preterm delivery is a history of preterm delivery in a prior pregnancy [26].

Prematurity is a major contributor to neonatal and infant mortality [27].

- The risk of neonatal morbidity and mortality decreases as gestational age at birth increases [27].

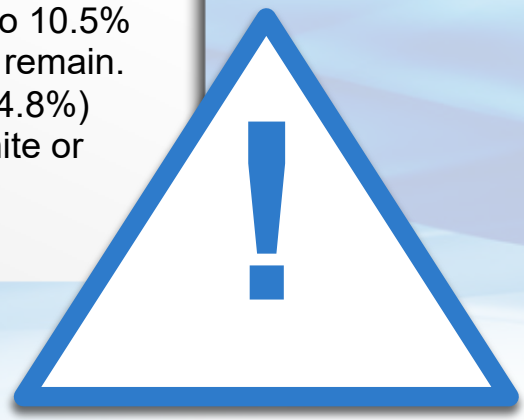
Defining Early Birth	
Extreme preterm delivery	Delivery prior to 28w0d gestation
Early preterm delivery	Delivery between 28w0d and 33w6d
Late preterm delivery	Delivery between 34w0d and 36w6d

PTL occurs due to four major pathologic pathways:

- **Intrauterine infection**
- **Decidual hemorrhage**
- **Excessive uterine stretch**
- **Maternal or fetal stress**

RISK FACTORS

- There are numerous risk factors for preterm delivery (Table: **Risk Factors for Preterm Birth**).
- Some risk factors are modifiable, others are not.
- There are several theories regarding the etiology for preterm labor and there are likely different mechanisms for various groups of women [1].
- In 2021, preterm birth affected about 1 of every 10 infants born in the United States. The preterm birth rate rose 4% in 2021, from 10.1% in 2020 to 10.5% in 2021. However, racial and ethnic differences in preterm birth rates remain. In 2021, the rate of preterm birth among African-American women (14.8%) was about 50 percent higher than the rate of preterm birth among white or Hispanic women (9.5% and 10.2% respectively) [28].



Risk Factors for PTB

Maternal Characteristics

- African American race
- Low pre-pregnancy BMI
- Tobacco use
- Substance use
- Periodontal disease

Pregnancy Complications

- Vaginal bleeding
- Short cervix
- Urinary tract infection
- Genital tract infection
- Systemic infection
- Sepsis
- Assisted reproductive technologies

Social and Economic Factors

- Social disadvantage
- Economic disadvantage
- Low educational achievement
- Lack of access to prenatal care
- Residence in disadvantaged area

Click each box for more details.

Medical History

- Prior LEEP or cold knife cone
- Mullerian anomaly

Obstetric History

- Prior preterm delivery
- Short interpregnancy interval
- Multiple gestation

PTL typically presents with similar symptoms as term labor. Early symptoms are typically non-specific and can be present for several hours before a woman presents for evaluation. The symptoms may include any of the following:

- Menstrual-like cramping
- Mild, irregular contractions
- Low back ache
- Vaginal pressure
- Vaginal discharge

Diagnostic Challenges

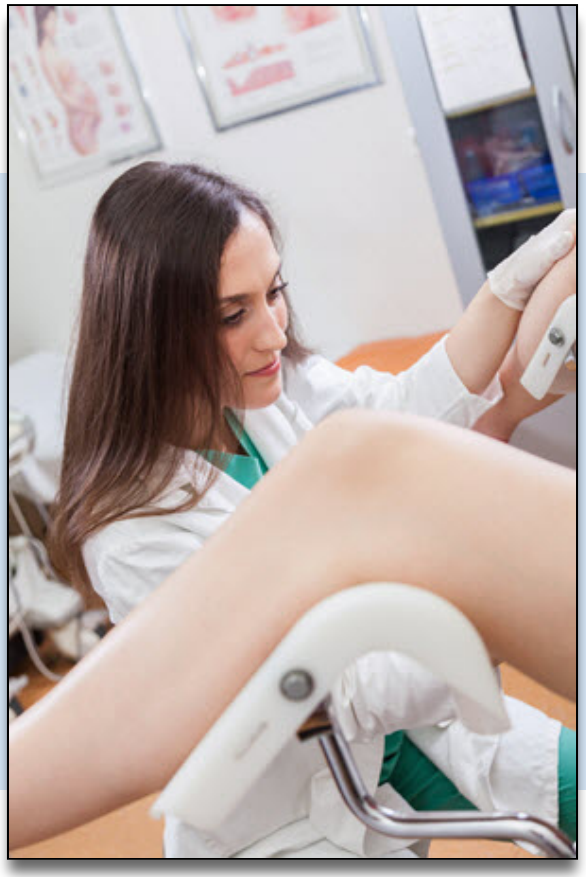
- Symptoms of PTL are typically present transiently in all normal pregnancies
- Signs that the symptoms may be indicative of true preterm labor include increased:
  - Duration of symptoms
  - Frequency of symptoms
  - Intensity of symptoms
- Only 13 percent of patients presenting at <34 weeks of gestation who meet explicit contraction criteria for PTL give birth within one week [29].

The initial evaluation of women with suspected PTL includes:

- Review the patient's:
  - Obstetrical history
  - Medical history
  - Gestational age
- Maternal vital signs.
- Evaluate fetal heart rate tracing.
- Assess contraction frequency, duration, and intensity.
- Examine the uterus to assess firmness, tenderness, fetal size, and fetal position.
- Perform speculum exam to evaluate for vaginal discharge and to assess cervical appearance.
  - Avoid using lubricants given they can interfere with diagnosis of rupture of membranes (ROM).
- Consider obtaining a fetal fibronectin (fFN) swab.
- Consider obtaining a cervical length ultrasound
- Perform a digital cervical exam.
  - Assess the dilation and effacement of the cervix, fetal station, cervical consistency and cervical position.
- Review prior ultrasound reports with particular attention to placental location

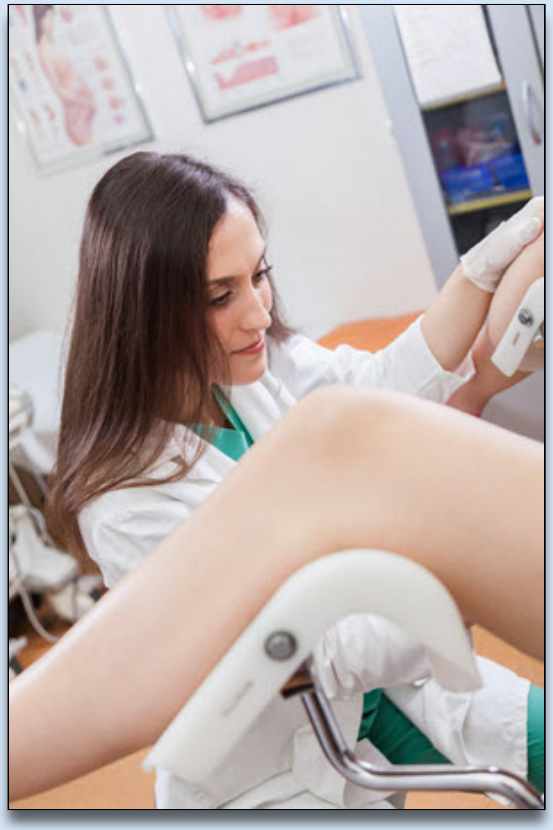
Obtain a cervicovaginal fluid specimen in case fFN testing is desired. If a speculum is not available a blind collection can be performed.

- There are different methods to obtain specimens:
  - Depress the posterior vaginal wall with an unlubricated, gloved finger then pass the polyester swab slowly along the finger towards the posterior fornix until resistance is felt [1].
  - Hold the labia apart, then pass the swab blindly into the vagina, directing slowly towards the posterior fornix until resistance is met [2].
- The swab is rotated in the posterior fornix for 10 seconds.
- In both methods, it is important to stop at the first sign of resistance to avoid rupturing exposed membranes, if present.



The goals of the initial examination are to:

- Assess for uterine bleeding.
- Evaluate for intact or ruptured membranes.
- Determine cervical dilation.
- Evaluate for ruptured membranes by speculum exam.
  - Preterm premature rupture of membranes (PPROM) often precedes or occurs during PTL.
  - Diagnosis and management of PPROM are reviewed separately.



Speculum Exam

Any woman who presents with concern for PTL should be evaluated by speculum exam prior to digital cervical exam. The exam should evaluate for:

- Hourglassing membranes
  - Diagnosed based on the amniotic sac protruding into the vagina through a cervix with limited dilation
  - Typically seen when dilation is <5 cm
- Bleeding
- ROM
  - Evaluate for nitrazine, pooling, ferning, if indicated
  - Consider Amnisure if equivocal testing and high clinical suspicion for ROM
- Vaginal infection
  - Collect gonorrhea, chlamydia, yeast and wet mount testing, as indicated
  - Consider obtaining group B streptococcus (GBS) culture
- Collect fFN

Cervical Examination

Cervical evaluation should only occur once the following have been excluded by the necessary means (i.e. US, history, physical exam, labs, etc.):

- Placenta previa
- ROM

Once these have been ruled out, the cervix may be evaluated by digital exam for dilation and effacement.

The cervical evaluation should occur quickly if the information is urgently needed to provide care for the patient, such as abnormal FHR or suspicion of active labor.

Laboratory Evaluation

Ordering the following laboratory tests may be considered:

- Vaginal-rectal GBS culture if not done within the previous five weeks.
  - CBC with differential
  - Type and screen
- Urine culture, since asymptomatic bacteriuria is associated with an increased risk of preterm labor and birth.
- Drug testing in patients with risk factors for substance abuse. There is an association between cocaine use and placental abruption.
- fFN in women < 34 weeks of gestation with cervical dilation < 3 cm and cervical length 20 to 30 mm on transvaginal ultrasound examination.
- If not already performed, consider testing for sexually transmitted infections (STI), gonorrhea and chlamydia.

FETAL FIBRONECTIN

fFN is an extracellular matrix protein present at the decidual-chorionic interface.

Disruption of the decidual-chorionic interface due to subclinical infection, inflammation, abruption, or uterine contraction leads to the release of fFN into the cervico-vaginal secretions. This is the basis for fFN as a marker for predicting spontaneous preterm birth [3].

A + fFN concentration correlates to 50 ng/mL or higher in cervico-vaginal fluid between 22 0/7 weeks and 34 6/7 weeks gestation.

Click the left and right arrows to see more.

FETAL FIBRONECTIN

fFN can be utilized to help distinguish women in true preterm labor from those with false labor.

fFN does not add to the predictive value in women with a cervical length measuring <20 mm or >30 mm.

- In these situations, the predictive value of the CL ultrasound is great enough to either withhold or initiate treatment for preterm labor without the adjunct of the fFN
- However, if the CL measures 20-30 mm, fFN can be helpful in deciding management

fFN testing may help to avoid unnecessary intervention and associated costs for 20-50% of women who will go on to delivery at term without tocolysis [4].

Click the left and right arrows to see more.

FETAL FIBRONECTIN

Research has shown that fFN testing demonstrates the following sensitivity and specificity regarding outcomes in the setting of threatened preterm labor [5]:

Gestation	Sensitivity	Specificity
Delivery within 7-10 days	76.7	82.7
Delivery < 34 weeks	69.1	84.4
Delivery < 37 weeks	60.8	82.3

Click the left and right arrows to see more.

FETAL FIBRONECTIN

Positive and negative predictive values of a test suggest how good the test is at ruling in or ruling out a potential outcome in a specific population.

For fFN, the positive predictive value is relatively poor at 13-36% while the negative predictive value is excellent at >95% [14].

- This indicates that in a women with a negative test, the chance that she will deliver within 7 days of a negative test is <5%

Click the left and right arrows to see more.

FETAL FIBRONECTIN

False positive fFN results can occur due to [6-8]:

- Ejaculate from coitus within the previous 24 hours
- A grossly bloody specimen
- Digital cervical examination

Transvaginal US is unlikely to cause a false positive result according to a study of 310 women with a negative baseline fFN test had a second negative fFN test post ultrasound coordinating in 92% [9].

Substances placed vaginally may also interfere with the fFN assay [10]:

- Lubricants
- Medications
- Douching

Click the left and right arrows to see more.

FETAL FIBRONECTIN

Qualitative tests involve the threshold of 50 ng/mL and when compared to quantitative control of fFN the predictive value is improved [11-13].

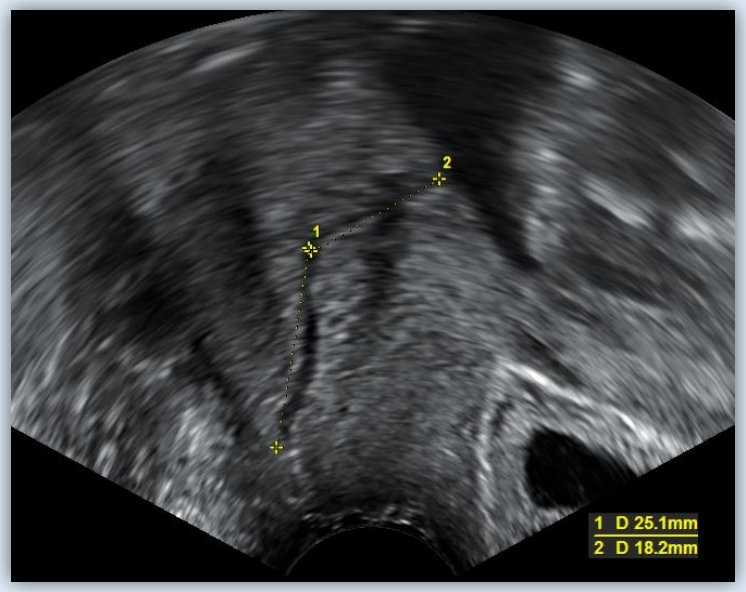
Currently, in the United States, however, the instruments are not available for quantitative measures of fFN.

Click the left and right arrows to see more.

FETAL FIBRONECTIN

Cervical Length Ultrasound

- In patient's who present with concern for PTL, after obtaining a fFN swab and performing a digital cervical exam, consider performing a cervical length US if the woman is <2 cm dilated



Click the next button to continue the course.

Cervical Length Ultrasound

Consider performing an obstetrical US examination to look for:

- Fetal, placental, and maternal structural abnormalities
- Confirm the fetal presentation
- Assess amniotic fluid volume and estimate fetal weight
- Consider obtaining a cervical length US

- Measurement of cervical length is useful for supporting or excluding the diagnosis of PTL when the diagnosis is unclear.
- A short cervix before 32 weeks of gestation is predictive of preterm birth in all populations.

Click each button to learn more.

If the cervical length is...

< 20 mm	20-30 mm	> 30 mm

Recommend admission for management of PTL

- Symptomatic women with cervical length < 20 mm are at high risk (> 25%) of delivery within seven days.
- The addition of fFN testing does not significantly improve the predictive value of cervical length measurement alone [16-18,20,21].
- To reduce morbidity associated with preterm birth, beginning interventions is reasonable without waiting for the fFN testing result.

Click each button to learn more.

If the cervical length is...

< 20 mm	20-30 mm	> 30 mm

Cervical length 20-30 mm

- Symptomatic women with cervical dilation < 30 cm and cervical length 20 to 30 mm are at increased risk of preterm birth compared with women with longer cervical lengths, but most of these women do not deliver preterm.
  - Therefore, for this subgroup of women, a cervicovaginal sample for fFN testing can be sent.
- Selective testing helps reduce diagnostic uncertainty and, in turn, unnecessary intervention, by identifying the significant proportion of patients in this group who are at low (< 5%) risk of preterm delivery within seven days [15].
- With fFN testing being expensive, a reduction of women tested by one third is advantageous [17, 18].
- When the fFN is positive, it is reasonable to initiate interventions to reduce morbidity associated with preterm birth.
- If the fFN test is negative, discharging the patient after 6 to 12 hours of observation, given its high negative predictive value (98 to 100% for delivery within 7 or 14 days [19]) is reasonable [4].
- Use of sonographic cervical length and fFN determinations to differentiate true labor from false labor in preterm symptomatic women are supported by the American College of Obstetricians and Gynecologists (ACOG)[20] and Society for Maternal Fetal Medicine (SMFM) [25].

Click each button to learn more.

If the cervical length is...

< 20 mm	20-30 mm	> 30 mm

Discharge Home

Symptomatic women with cervical lengths measuring > 30 mm have a < 5% risk of delivery within 7 days.

- The addition of fFN testing does not significantly improve the predictive value of cervical length measurement alone [16, 17, 21, 22].
- Do not recommend sending fFN.

Evaluate for any alternative etiologies for the woman's symptoms. If no etiology is found and the CL is > 30 mm, the woman can be discharged home.

Encourage the woman to return for evaluation with:

- Worsening contractions
- Bleeding
- ROM Decreased fetal
- movement

The diagnosis of PTL occurs from regular painful uterine contractions along with cervical change based upon:

- Dilation

  and/or

- Effacement

The clinical findings of early labor are poorly predictive of the diagnosis, thus over diagnosing is common until labor is well established.

Management of PTL

- Depends on gestational age and etiology
- If there is no clear etiology for preterm labor and a patient is less than 34 weeks, typical management includes:
  - Tocolysis
  - Antenatal corticosteroids
  - Magnesium sulfate if <32 weeks
  - Collect GBS culture
  - GBS antibiotics
- If there is no clear etiology for PTL and a patient is 34 weeks or above, typical management includes:
  - Expectant management
- Regardless of gestational age, if the facility cannot safely care for a neonate at the gestational age of maternal presentation, transfer should be coordinated

Management of Preterm Labor

Contraindications to tocolysis: [23]

- Chorioamnionitis
- Lethal fetal anomaly
- Intrauterine fetal demise
- Nonreassuring fetal status
- Severe preeclampsia or eclampsia
- Maternal bleeding with hemodynamic instability
- Preterm premature rupture of membranes, although tocolysis may be considered for purpose of maternal transportation, steroid administration or both
- Maternal contraindications to tocolysis (medication specific)

Management of Preterm Labor < 34 Weeks [2, 18, 20, 23, 24, 25]

Tocolysis

- Indomethacine initiate 50 to 100 mg orally or rectally, followed by 25 mg every 4 to 6 hours orally in women between 24 and 32 weeks' gestation. Duration of treatment is generally limited to 48 to 72 hours [23, 30,31].
- If > 32 weeks, initiate nifedipine. Immediate release: Initial: 20 to 30 mg as a loading dose, followed by 10 to 20 mg every 3 to 8 hours for up to 48 hours; maximum dose: 180 mg/day until antenatal corticosteroids is complete [23].

Antenatal corticosteroids

- Given to reduce neonatal morbidity and mortality associated with preterm birth.
- Administer betamethasone 12 mg every 24 hours for a total of 2 doses [23]. A single course of betamethasone is recommended for women between 24 and 34 weeks' gestation, including those with ruptured membranes or multiple gestations, who are at risk of delivering within 7 days. A single course may be appropriate in some women beginning at 23 weeks' gestation or late preterm (between 34 0/7 weeks' and 36 6/7 weeks' gestation). A single repeat course may be considered in some women with pregnancies less than 34 weeks' gestation at risk for delivery within 7 days and who had a course of antenatal corticosteroids >14 days prior [23, 32, 33].

Management of Preterm Labor < 34 Weeks [2, 18, 20, 23, 24, 25]

Magnesium sulfate if <32 weeks

- Given as neuroprotection to prevent cerebral palsy associated with preterm birth.
- Administer magnesium sulfate with a 4 g intravenously bolus over 20 minutes followed by maintenance dose of 1 g/hour [23, 34].

Collect GBS culture

GBS antibiotics [35]

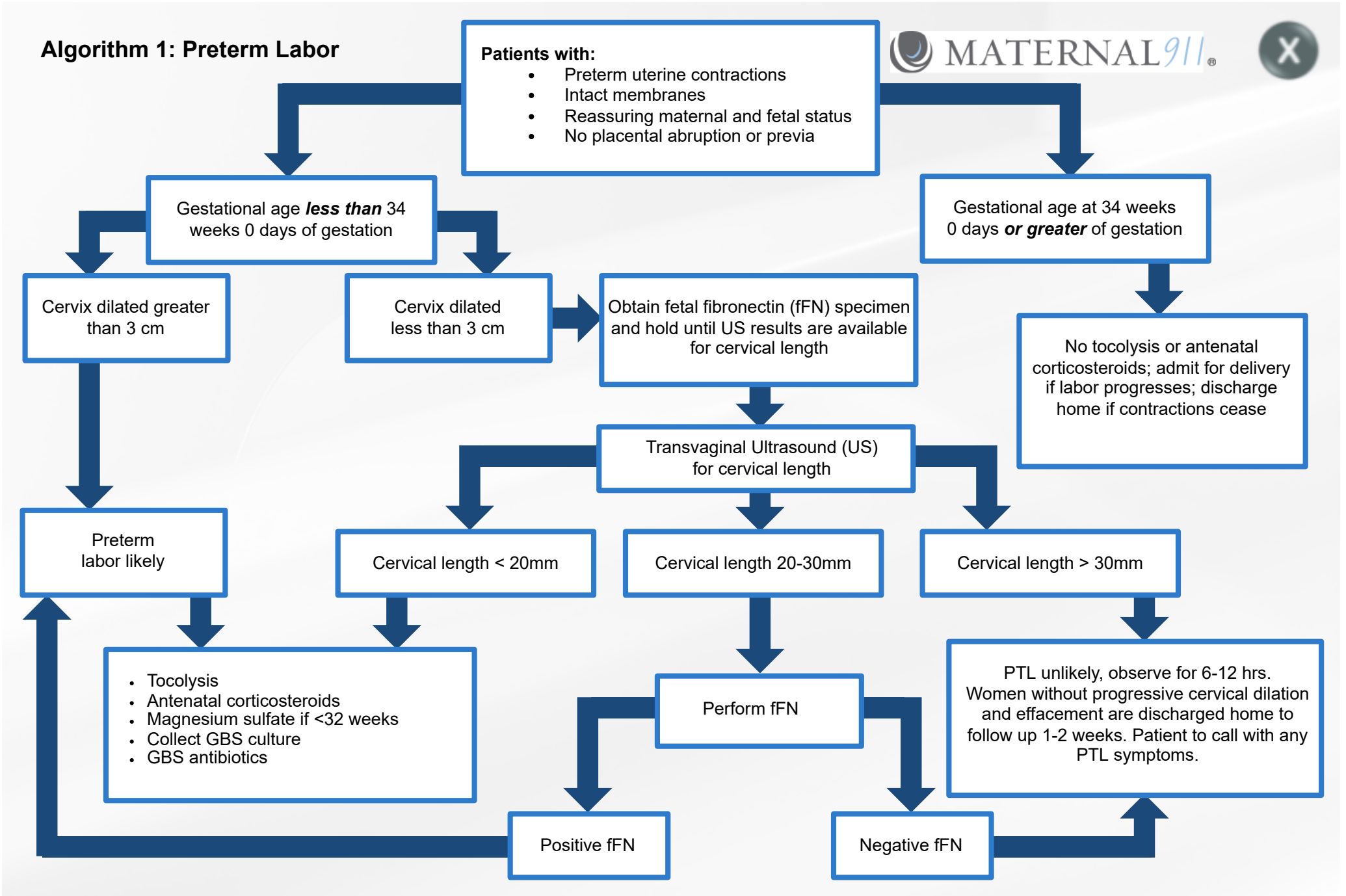
- Penicillin G 5 million units IV followed by 2.5 to 3 million units q 4 hours until contractions cease or delivery occurs.
- Ampicillin 2 g IV followed by 1 g q 4 hours can be used if penicillin is not available.
- If the patient has a low risk penicillin allergy, Ancef 2 g IV followed by 1g q8 hours can be used.
- If the patient has a high risk penicillin allergy, Vancomycin 20 mg/kg q8 hours can be used. Vancomycin 20 mg/kg q8 hours can be used or Clindamycin 900 mg intravenously every eight hours until delivery

Please review Algorithm 1

< 34 Weeks of Gestation

2 of 2

Algorithm 1: Preterm Labor



≥ 34 Weeks of Gestation

Management of Preterm Labor ≥ 34 Weeks

If there is evidence of preterm labor, admit for expectant management

- Tocolysis is not indicated
- Magnesium sulfate is not indicated
- Antenatal corticosteroids should be administered if not given previously in pregnancy
- Collect GBS culture
- GBS antibiotics as indicated

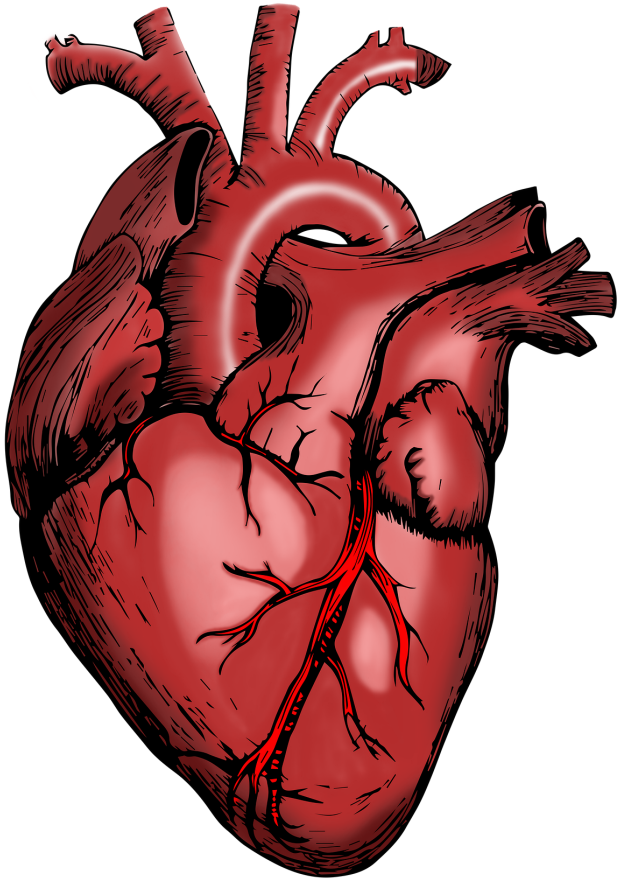
Prevention of Preterm Birth [24]:

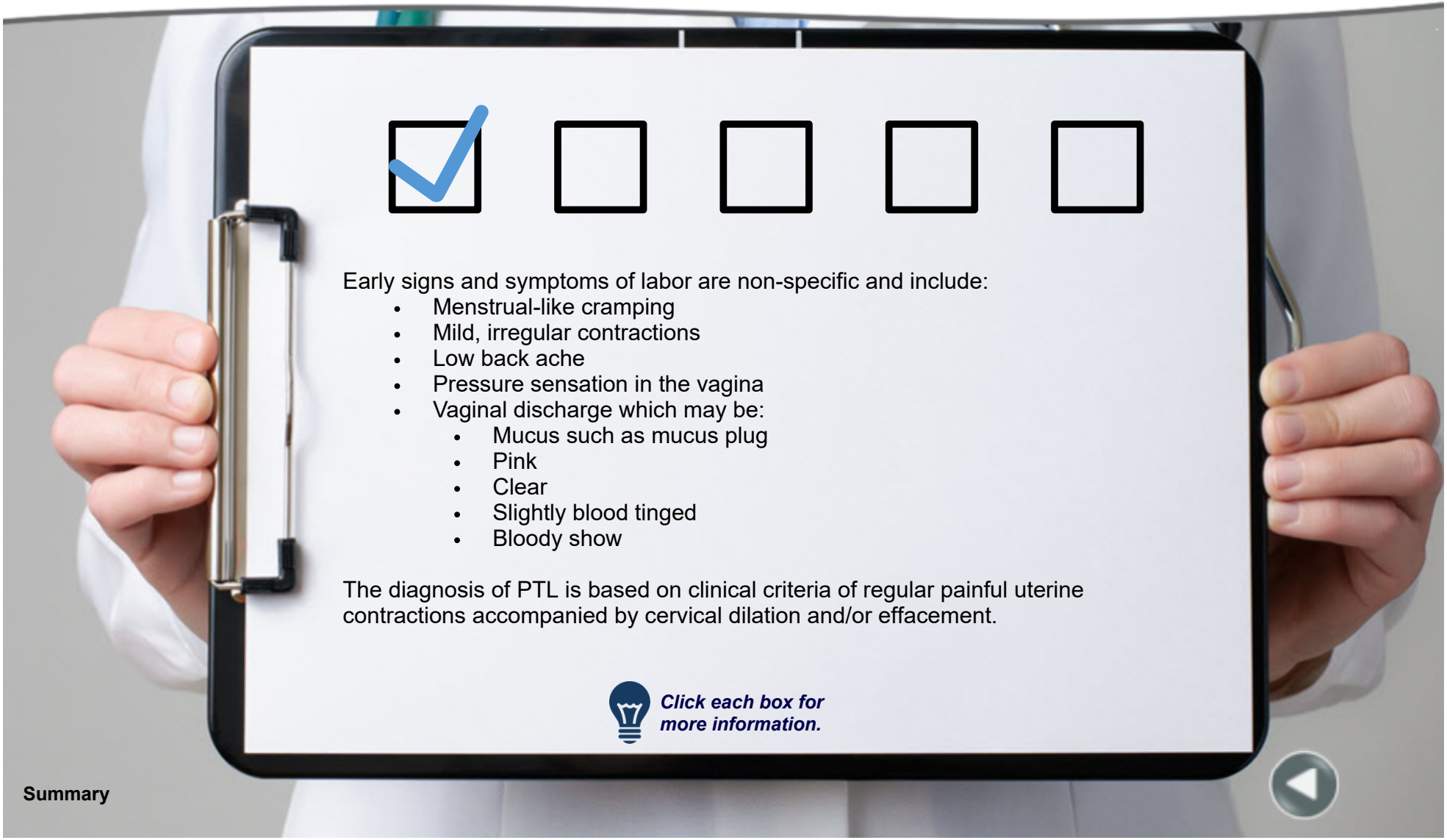
- Smoking cessation.
- Reduction of multiple gestation by limiting the number of embryo transfers in women undergoing assisted reproductive technology or multifetal pregnancy reduction.
- Prior Spontaneous Preterm Delivery
  - Progesterone supplementation starting at 16 weeks gestation
  - Cervical length ultrasound surveillance from 16-24 weeks
  - Cerclage if cervical length measures <25 mm
- No Prior Spontaneous Preterm Delivery
  - Measure cervical length at the time of anatomy US
  - Begin progesterone supplementation if cervical length measures <25 mm
  - Cerclage if cervical length measures <10 mm

Cardiovascular Risk

An increased risk of maternal cardiovascular disease exists for years in women with spontaneous preterm birth (sPTB) compared to those without this history.

- It may be useful for women with this history to be identified by their primary care providers and encouraged to optimize modifiable risk factors for cardiovascular health; it is unclear why sPTB is a marker for later cardiovascular disease compared to women without this history.





Early signs and symptoms of labor are non-specific and include:

- Menstrual-like cramping
- Mild, irregular contractions
- Low back ache
- Pressure sensation in the vagina
- Vaginal discharge which may be:
  - Mucus such as mucus plug
  - Pink
  - Clear
  - Slightly blood tinged
  - Bloody show

The diagnosis of PTL is based on clinical criteria of regular painful uterine contractions accompanied by cervical dilation and/or effacement.

Click each box for more information.

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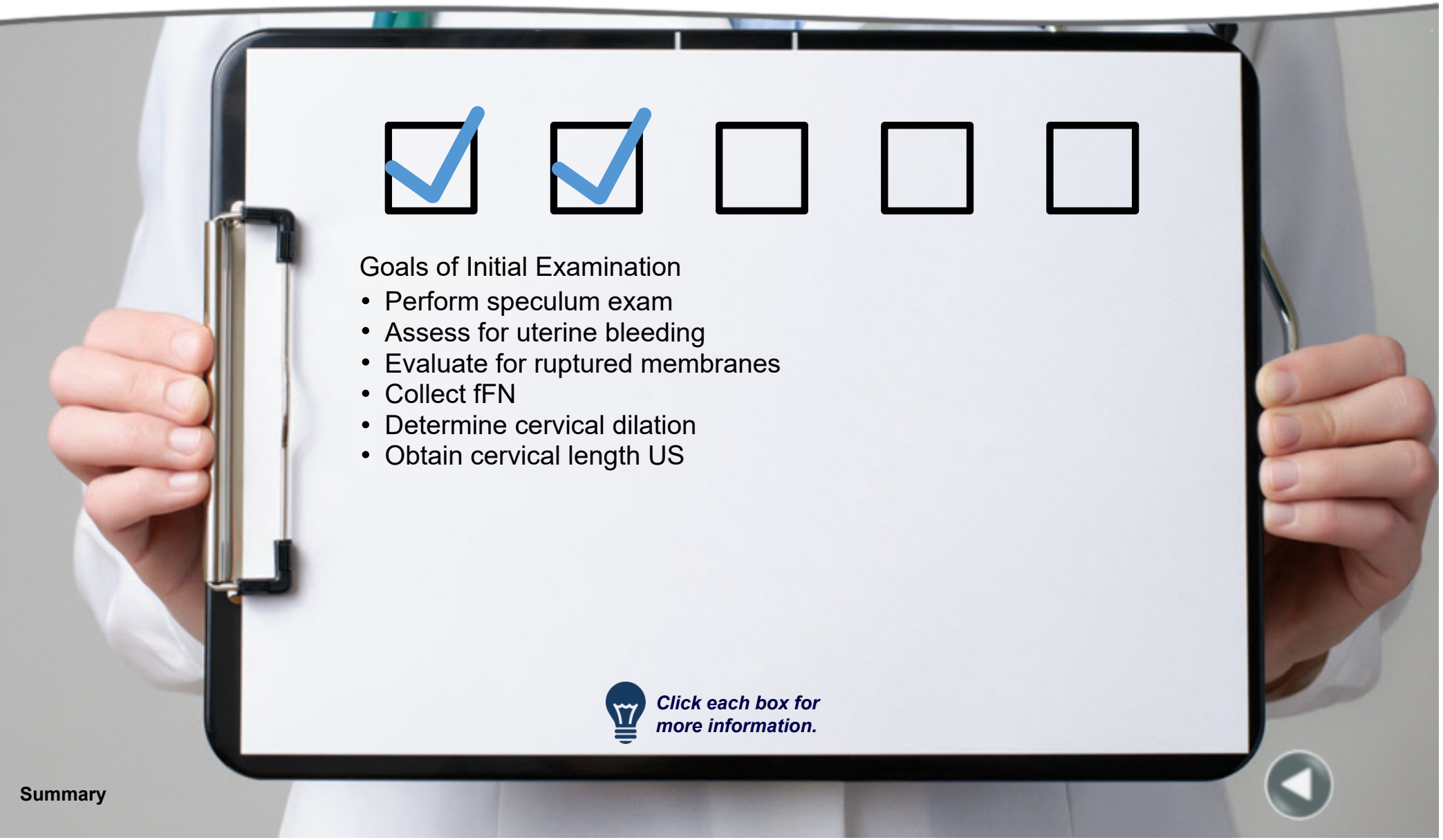
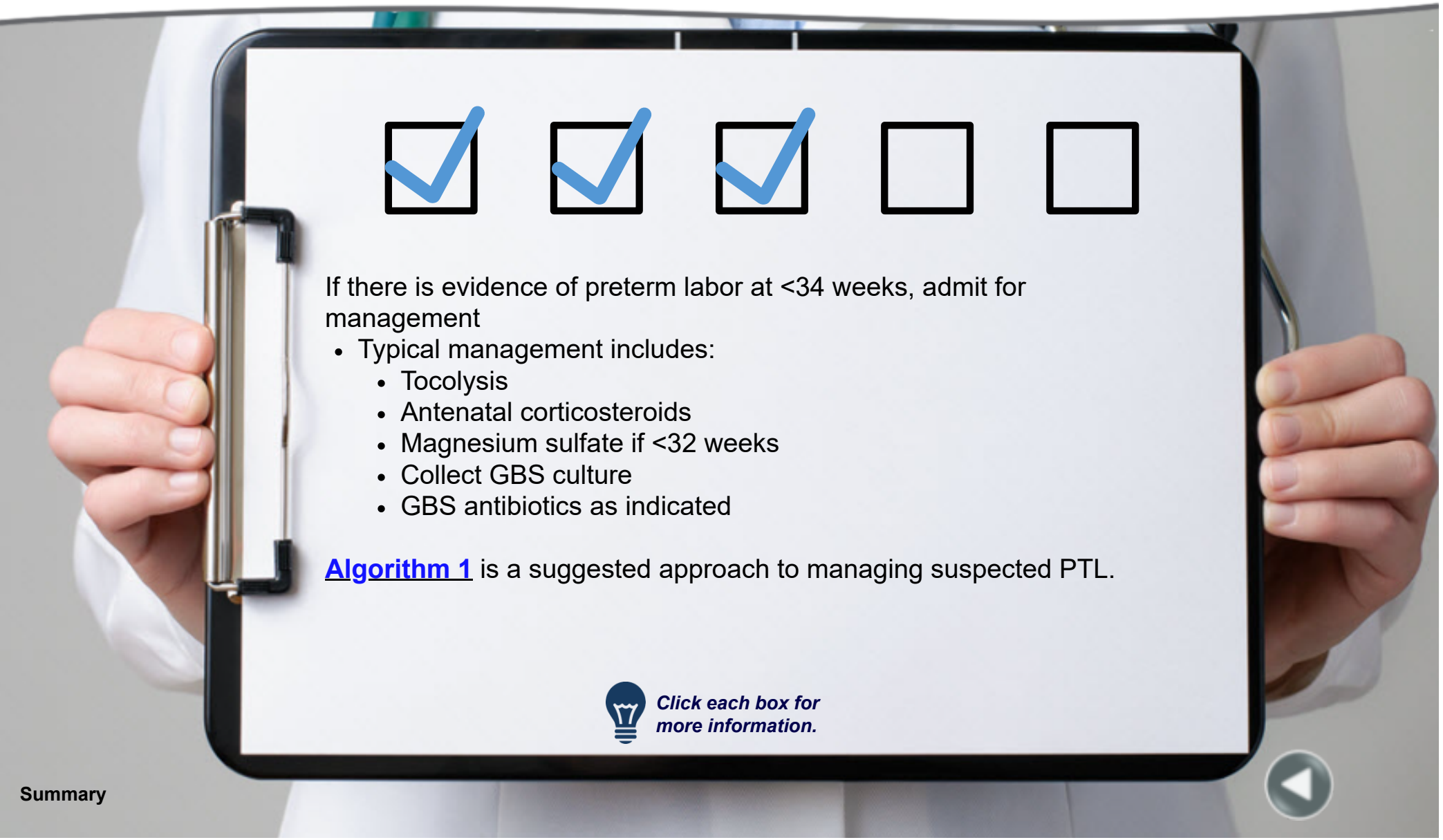


Goals of Initial Examination

- Perform speculum exam
- Assess for uterine bleeding
- Evaluate for ruptured membranes
- Collect fFN
- Determine cervical dilation
- Obtain cervical length US

Click each box for more information.

Summary



If there is evidence of preterm labor at <34 weeks, admit for management

- Typical management includes:
  - Tocolysis
  - Antenatal corticosteroids
  - Magnesium sulfate if <32 weeks
  - Collect GBS culture
  - GBS antibiotics as indicated

Algorithm 1 is a suggested approach to managing suspected PTL.

Click each box for more information.

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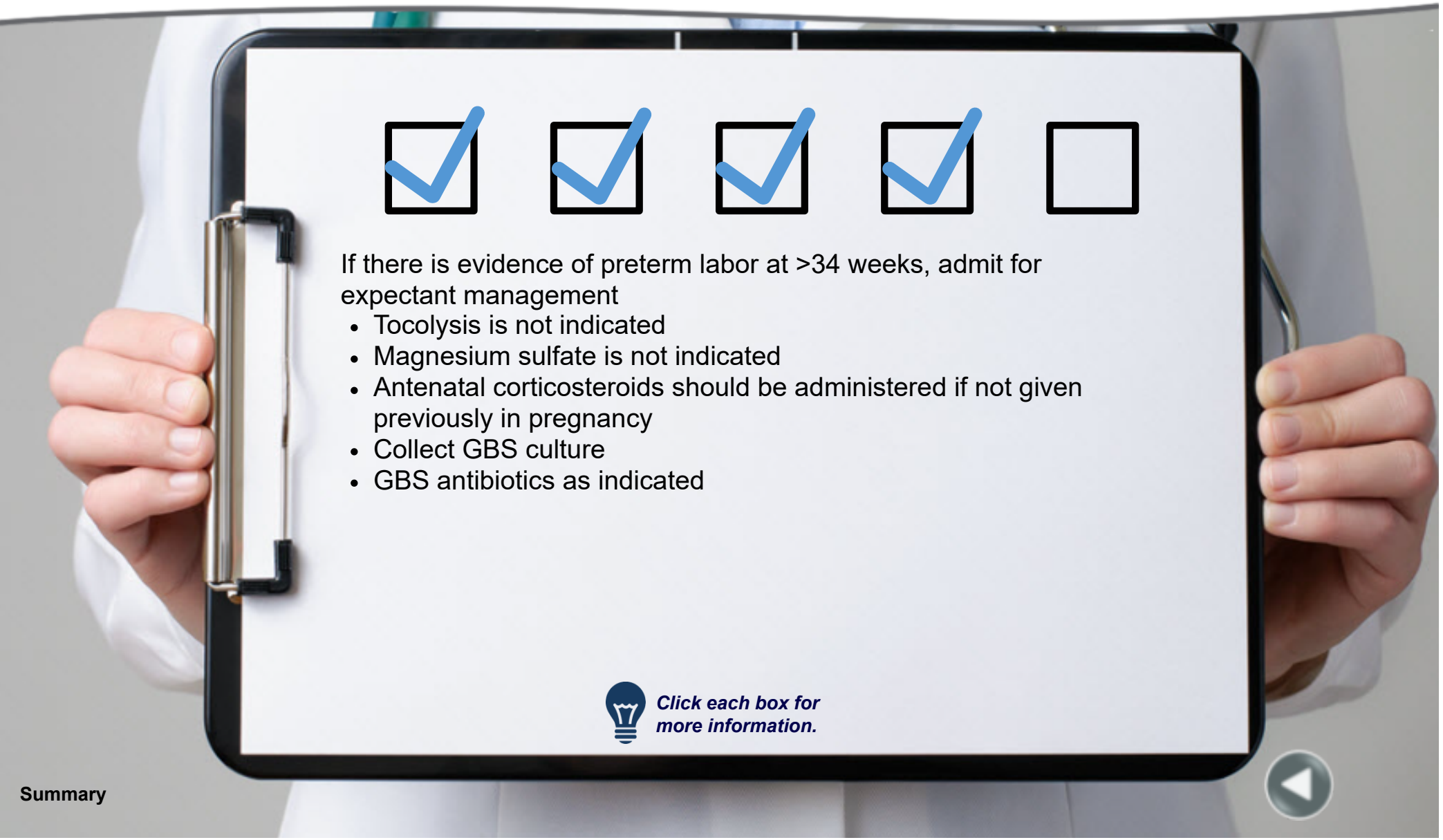
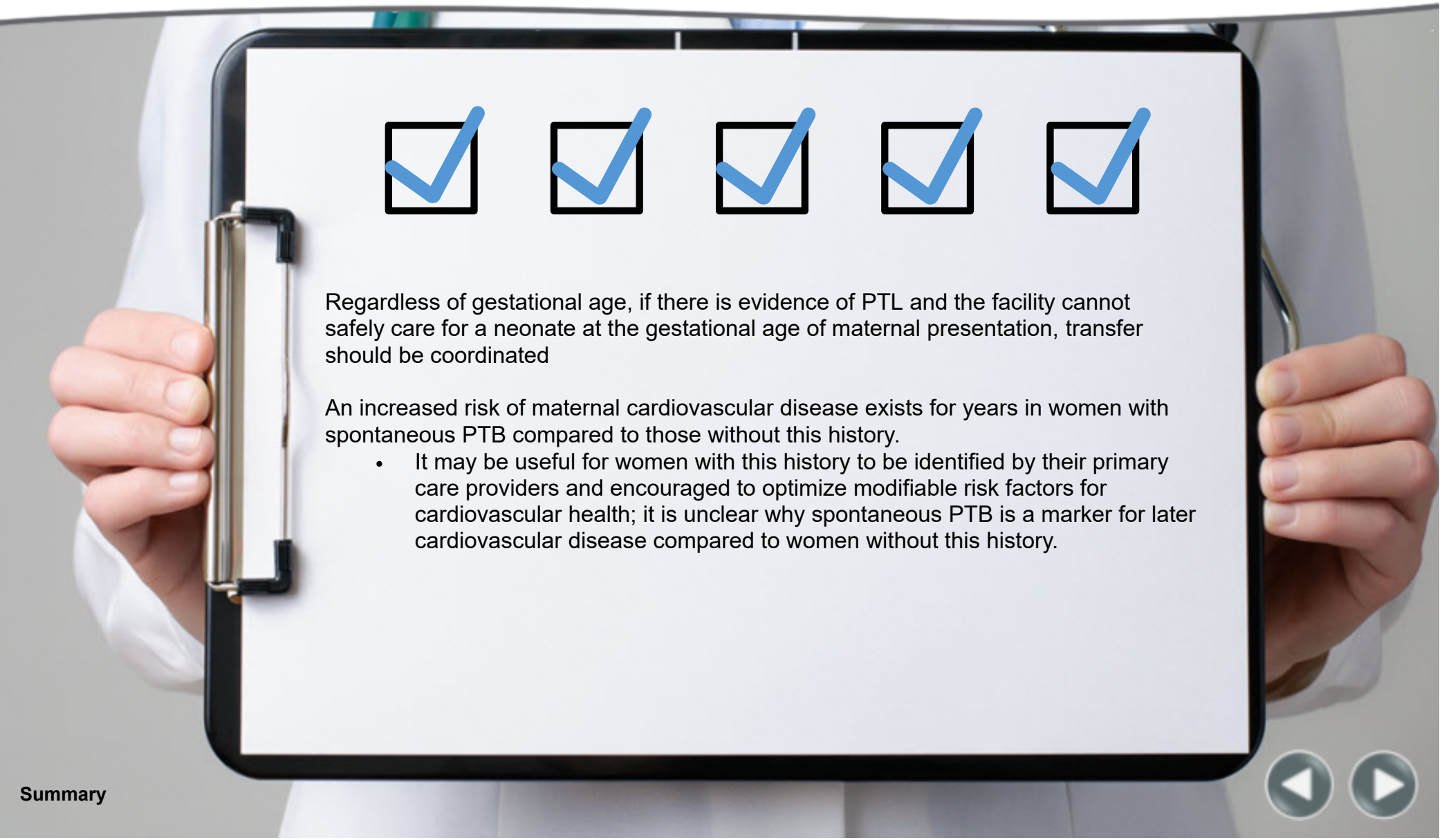


If there is evidence of preterm labor at >34 weeks, admit for expectant management

- Tocolysis is not indicated
- Magnesium sulfate is not indicated
- Antenatal corticosteroids should be administered if not given previously in pregnancy
- Collect GBS culture
- GBS antibiotics as indicated

Click each box for more information.



Regardless of gestational age, if there is evidence of PTL and the facility cannot safely care for a neonate at the gestational age of maternal presentation, transfer should be coordinated

An increased risk of maternal cardiovascular disease exists for years in women with spontaneous PTB compared to those without this history.

- It may be useful for women with this history to be identified by their primary care providers and encouraged to optimize modifiable risk factors for cardiovascular health; it is unclear why spontaneous PTB is a marker for later cardiovascular disease compared to women without this history.

Congratulations!

You have successfully completed this module.

Click on the above 'X' to take the post-test for this course.
If you do not attain a passing score after two attempts at the post-test the entire program must be repurchased.

1. Stafford IP, Garite TJ, Dildy GA, et al. A comparison of speculum and nonspeculum collection of cervicovaginal specimens for fetal fibronectin testing. Am J Obstet Gynecol 2008; 199:131.e1.

2. Roman AS, Koklanaris N, Paidas MJ, et al. "Blind" vaginal fetal fibronectin as a predictor of spontaneous preterm delivery. Obstet Gynecol 2005; 105:285.

3. Feinberg RF, Kliman HJ, Lockwood CJ. Is oncofetal fibronectin a trophoblast glue for human implantation? Am J Pathol 1991; 138:537.

4. Haas DM, Imperiale TF, Kirkpatrick PR, et al. Tocolytic therapy: a meta-analysis and decision analysis. Obstet Gynecol 2009; 113:585.

5. Deshpande SN, van Asselt AD, Tomini F, et al. Rapid fetal fibronectin testing to predict preterm birth in women with symptoms of premature labour: a systematic review and cost analysis. Health Technol Assess 2013; 17:1.

6. McKenna DS, Chung K, Iams JD. Effect of digital cervical examination on the expression of fetal fibronectin. J Reprod Med 1999; 44:796.

7. McLaren JS, Hezelgrave NL, Ayubi H, et al. Prediction of spontaneous preterm birth using quantitative fetal fibronectin after recent sexual intercourse. Am J Obstet Gynecol 2015; 212:89.e1.

8. Shimoya K, Hashimoto K, Shimizu T, et al. Cervical fluid oncofetal fibronectin as a predictor of early ectopic pregnancy. Is it affected by blood contamination? J Reprod Med 2002; 47:640.

9. Turitz, AL, Ackerman, CM, Johnson, DL et al. A comparison of prevaginal and postvaginal manipulation fetal fibronectin. Am J Obstet Gynecol 2016. 214:646.e1-6.

10. http://www.ffntest.com/pdfs/rapid_ffn_product_insert_lettersize.pdf

11. Abbott DS, Radford SK, Seed PT, et al. Evaluation of a quantitative fetal fibronectin test for spontaneous preterm birth in symptomatic women. Am J Obstet Gynecol 2013; 208:122.e1.

12. Kuhrt K, Unwin C, Hezelgrave N, et al. Endocervical and high vaginal quantitative fetal fibronectin in predicting preterm birth. J Matern Fetal Neonatal Med 2014; 27:1576.

13. Kuhrt K, Hezelgrave N, Foster C, et al. Development and validation of a predictive tool for spontaneous preterm birth, incorporating quantitative fetal fibronectin, in symptomatic women. Ultrasound Obstet Gynecol 2015.

14. Daskalakis GJ, Papantoniou NE, Koutsodimas NB, Papapanagiotou A, Antsaklis AJ. Fetal fibronectin as a predictor of preterm birth. J Obstet Gynaecol. 2000 Jul;20(4):347-53. doi: 10.1080/01443610050111922. PMID: 15512582

15. Tsoi E, Fuchs IB, Rane S, et al. Sonographic measurement of cervical length in threatened preterm labor in singleton pregnancies with intact membranes. Ultrasound Obstet Gynecol 2005; 25:353.

16. van Baaren GJ, Vis JY, Wilms FF, et al. Predictive value of cervical length measurement and fibronectin testing in threatened preterm labor. Obstet Gynecol 2014; 123:1185.

17. Schmitz T, Maillard F, Bessard-Bacquaert S, et al. Selective use of fetal fibronectin detection after cervical length measurement to predict spontaneous preterm delivery in women with preterm labor. Am J Obstet Gynecol 2006; 194:138.

18. Audibert F, Fortin S, Delvin E, et al. Contingent use of fetal fibronectin testing and cervical length measurement in women with preterm labour. J Obstet Gynaecol Can 2010; 32:307.

19. Foster C, Shennan AH. Fetal fibronectin as a biomarker of preterm labor: a review of the literature and advances in its clinical use. Biomark Med 2014; 8:471.

20. Committee on Practice Bulletins—Obstetrics, The American College of Obstetricians and Gynecologists. Practice bulletin no. 130: prediction and prevention of preterm birth. Obstet Gynecol 2012; 120:964.

21. Gomez R, Romero R, Medina L, et al. Cervicovaginal fibronectin improves the prediction of preterm delivery based on sonographic cervical length in patients with preterm uterine contractions and intact membranes. Am J Obstet Gynecol 2005; 192:350.

22. Hincz P, Wilczynski J, Kozarzewski M, Szaflik K. Two-step test: the combined use of fetal fibronectin and sonographic examination of the uterine cervix for prediction of preterm delivery in symptomatic patients. Acta Obstet Gynecol Scand 2002; 81:58.

23. American College of Obstetricians and Gynecologists, Committee on Practice Bulletins-Obstetrics. ACOG Practice Bulletin No. 171: Management of preterm labor. Obstet Gynecol. 2016;128(4):e155-e164. doi:10.1097/AOG.0000000000001711.

24. Chang HH, Larson J, Blencowe H, et al. Preventing preterm births: analysis of trends and potential reductions with interventions in 39 countries with very high human development index. Lancet 2013; 381:223.

25. Society for Maternal Fetal Medicine (SMFM). Electronic address: pubs@SMFM.org, McIntosh J, Feltovich H, et al. The role of routine cervical length screening in selected high and low risk women for preterm birth prevention. Am J Obstet Gynecol 2016; 215:B2.

26. Robinson, J.N., & Norwitz, E. R. (2023). Spontaneous preterm birth: Overview of risk factors and prognosis. In V. Barss (ed.), *UpToDate.* Retrieved April 23, 2023, from https://www.uptodate.com/contents/spontaneous-preterm-birth-overrivew-of-risk-factores-and-prognosis

27. Zacharias, N. (2023). Perinatal mortality. In L. Wilkie (Ed.), *UpToDate.* Retrieved April 23, 2023, from https://www.uptodate.com/contents/perinatal-mortality

28. Centers for Disease Control and Prevention (2022, November 1). Preterm Birth. Retrieved April 23, 2023, from https://www.cdc.gov/reproductivehealth/maternalinfanthealth/pretermbirth.htm

29. Sotiriadis, A., Papatheodorou, S., Kavvadias, A., Makrydimas. G. (2010). transvaginal cervical length measurement for prediction of preterm birth in women with threatened preterm labor: a meta-analysis. Ultrasound Obstet Gynecol. 2010;35(1):54.

30. Rath W, Kehl S. Acute tocolysis - a critical analysis of evidence-based data. *Geburtshilfe Frauenheilkd*. 2018;78(12):1245-1255. doi: 10.1055/a-0717-5329 [PubMed HYPERLINK "https://www.uptodate.com/contents/indomethacin-drug-information/abstract-text/30655648/pubmed"30655648]

31. Reinebrant HE, Pileggi-Castro C, Romero CL, et al. Cyclo-oxygenase (COX) inhibitors for treating preterm labour. *Cochrane Database Syst Rev*. 2015;(6):CD001992. doi: 10.1002/14651858.CD001992.pub3 [PubMed HYPERLINK "https://www.uptodate.com/contents/indomethacin-drug-information/abstract-text/26042617/pubmed"26042617]

32. ACOG Committee on Practice Bulletins–Obstetrics. ACOG Practice Bulletin No. 217: Prelabor rupture of membranes. Obstet Gynecol. 2020;135(3):e80-e97.

33. ACOG Committee on Obstetric Practice. ACOG Committee Opinion No. 713: Antenatal corticosteroid therapy for fetal maturation. Obstet Gynecol. 2017;130(2):e102-e109.

34. Crowther CA, Hiller JE, Doyle LW, Haslam RR; Australasian Collaborative Trial of Magnesium Sulphate (ACTOMg SO4) Collaborative Group. Effect of magnesium sulfate given for neuroprotection before preterm birth: a randomized controlled trial. JAMA. 2003;290(20):2669-2676.

35. Prevention of Group B Streptococcal Early-Onset Disease in Newborns: ACOG Committee Opinion, Number 797. Obstet Gynecol. 2020;135(2):e51.