
AAPLOG Practice Bulletin No. 3: Previable Induction of Labor for Chorioamnionitis

American Association of Pro-Life Obstetricians & Gynecologists*

ABSTRACT: When intrauterine infection develops prior to viability, prognosis for the fetus is guarded. Previable parturition can be pursued when infection is present, but physicians must challenge themselves to do only what is indicated and avoid causing unnecessary effects by their methods of terminating pregnancy.

Background

Previable Intra-amniotic Infection and Inflammation

Infection or inflammation of fetal membranes, the amniotic fluid, and the placenta and cord, frequently referred to collectively as “intra-amniotic infection” or parsed into “chorioamnionitis” and “funisitis” (also recently styled “intraamniotic infection, inflammation, or both” or “triple I”) represents a range of clinical presentations with different outcomes across different gestational ages.¹⁻³ Intra-amniotic infection is currently the subject of significant research to shed light on the extreme variety in presentation, consequences, and need for treatment.^{1,4,5} Since “chorioamnionitis” is the more familiar term to most clinicians, it will be used in this document and updated as national standards change.

Chorioamnionitis arises from an ascending infection from the lower maternal genitourinary tract. Regardless of membrane status, chorioamnionitis is recognized and confirmed more often in earlier gestational ages.⁶ It is thought to be one of the causes of the pathophysiology of mid-trimester loss of non-anomalous fetuses.⁷ It may lead to serious maternal consequences including sepsis, abnormal labor curve, cesarean section, wound infection, cesarean hysterectomy, postpartum endometritis, postpartum hemorrhage, adult respiratory distress syndrome (ARDS), need for intensive care admission, and maternal death.^{5,8} Neonatal morbidity also increase in the setting of chorioamnionitis,

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and may result in excessive laboratory evaluation, unnecessary treatment, and admission to neonatal intensive care units.⁵ Diagnostic criteria proposed for chorioamnionitis are noted in Tables 1 and 2.^{5,9}

Table 1: Proposed criteria for “Triple I”	
Terminology	Features and Comments
Isolated Maternal Fever (“Documented” Fever)	Maternal oral temperature $\geq 39.0^{\circ}\text{C}$ (102.2°F) on any one occasion is “documented fever.” If the oral temperature $\geq 38.0^{\circ}\text{C}$ (100.4°F) but $\leq 39.0^{\circ}\text{C}$ (102.2°F), repeat the measurement in 30 minutes; if the repeat value, too remains $\geq 38.0^{\circ}\text{C}$ (100.4°F) it is “documented fever.”
Suspected Triple I	Fever without a clear source plus any of the following: <ul style="list-style-type: none"> <input type="checkbox"/> Baseline fetal tachycardia (> 160 bpm for 10 minutes or longer, excluding accelerations, decelerations and periods of marked variability) <input type="checkbox"/> Maternal WBC $> 15,000$ per mm^3 in absence of corticosteroids <input type="checkbox"/> Definite purulent fluid from the cervical os
Confirmed Triple I	All of the above plus <ul style="list-style-type: none"> <input type="checkbox"/> Amniocentesis-proven infection through a positive gram stain <input type="checkbox"/> Low glucose or positive amniotic fluid culture <input type="checkbox"/> Placental pathology revealing diagnostic features of infection
Adapted from Table 1: Features of Isolated Maternal Fever, and Triple I with Classification (from Higgins et al)	

There is a complex but well-established relationship between preterm premature rupture of membranes (PPROM), chorioamnionitis, and preterm delivery: rupture of membranes is a well-recognized risk factor for chorioamnionitis, but subclinical chorioamnionitis may be a cause of preterm labor and PPROM.^{10,11} While chorioamnionitis can occur in the presence of intact membranes,¹² it more commonly occurs with ruptured membranes. The longer the duration of ruptured membranes, the greater the likelihood of ascending infection. Histologic chorioamnionitis is found in 3-5% of term placentas and in 94% of placentas between 21-24 weeks of gestation.³

Table 2: Selected risk factors and their relative risks for chorioamnionitis		
Risk factor	Relative risk	Reference(s)
≥ 12 hours	5.8	13
> 18 hours	6.9	15
Prolonged labor		
Second stage > 2 hours	3.7	15
Active labor > 12 hours	4.0	14
Multiple digital exams with membrane rupture		
≥ 3 exams	2 to 5	13–14
Nulliparity	1.8	14
Group B streptococcus colonization	1.7 to 7.2	14, 16, 19
Bacterial vaginosis	1.7	17
Alcohol and tobacco use	7.9	15
Meconium-stained amniotic fluid	1.4–2.3	7, 14
Internal monitoring	2.0	13
Epidural anesthesia	4.1	15
Adapted from Tita and Andrews, 2010 Table 1.		

Previable Preterm Premature Rupture of Membranes

When rupture of membranes, an event normally occurring during term labor, occurs prior to the onset of labor and prior to 37 weeks gestation, it is termed preterm premature rupture of membranes (PPROM). The etiology of spontaneous PPRM is elusive, but likely relates to biochemical changes weakening the amnion and chorion.^{13,14} Separation of one membrane or of both (iatrogenic “pre-PPROM” or overt PPRM) may also occur iatrogenically after fetoscopy in 20% or more of cases.^{15,16} For the purposes of this document, spontaneous and iatrogenic PPRM will not be differentiated. Both are risk factors for intraamniotic infection although they behave differently due to the etiology and location of membrane rupture.¹⁵

Following PPRM, most women deliver within 14 days.¹⁷ Latency after PPRM is inversely proportional to gestational age: median latency in the midtrimester is 12 days (up to 37 days in one trial) while median latency in late preterm pregnancy is 1 day.¹⁸ Latency may also be affected by cervical length and amniotic fluid volume.^{19,20} When adjusted for gestational age, longer latency does

not correlate with improved survival, but prolonged latency does not worsen neonatal prognosis.¹⁷ Childhood outcomes, including school performance, are good compared to children born at similar gestational ages.¹⁸

Previaible preterm premature rupture of membranes (hereafter “previabile PPROM,” occasionally called “extreme PPROM”) is defined as rupture of membranes prior to 22-24 weeks’ gestational age. Previaible PPROM interferes with normal fetal lung maturation due to the absence of normal amniotic fluid volume, and also poses a significant risk for adverse outcomes due to the length of latency and likelihood of infection. In previous reviews of pregnancies with previabile PPROM between 20-23 weeks, 14% of women chose elective termination of pregnancy,²¹ 71% developed intrauterine infections,²¹ 36.4% of continued pregnancies result in stillbirth,²² and 44.9-48% of neonates died before 4 weeks of life or discharge.²¹⁻²³ The neonatal survival rate after previabile PPROM has improved over the past few decades and may be improved by an aggressive approach.²⁴

Childhood outcomes in previabile PPROM, unlike in PPROM after viability, are significantly worse and include poorer lung function, varying degrees of pulmonary hypertension, and learning difficulties.^{23,25} In addition, as many as one in seven women experience serious maternal morbidity during expectant management of previabile PPROM, including sepsis, intensive care unit admission, acute renal insufficiency, uterine curettage, hysterectomy, deep vein thrombosis, pulmonary embolus, blood transfusion, readmission, or maternal death.⁸

Like any abscess, chorioamnionitis requires not only broad-spectrum antibiotic coverage but also drainage or debridement of infected fluid and non-viable tissue. In the case of intrauterine infection, this entails termination of pregnancy and evacuation of infected membranes required for fetal life.

Ending Pregnancy with Second Trimester Abortion

In current mainstream guidelines, previabile PPROM is described as an indication for induced abortion of a singleton based on the maternal patient’s autonomy.²⁶ Depending on gestational age and physician experience, this may be carried out with mifepristone and misoprostol or with dilation and evacuation. However, higher abortion rates have not been shown to improve outcomes over expectant management.²⁷ There is not a significant body of literature on the maternal effects of termination of pregnancy for chorioamnionitis in the setting of previabile PPROM, but literature on termination of pregnancy for fetal anomaly may be helpful to consider. Termination of pregnancy for fetal anomaly can be associated with intensive grieving, so much that in one study twenty-two out of thirty women “just wanted to die.”²⁸ Post-traumatic stress and clinical depression has been noted in 44-49% and 28% of women, respectively; this improves to 20.5% and 13% after four months,^{29,30} but 20% of women continue to have symptoms for twelve months to 7 years.^{30,31} 2-2.7% of women experience regret.^{29,30}

Intraamniotic infection of the presenting twin is described as an indication for induced abortion based on beneficence.²⁶ A single study of dilation and evacuation of the presenting twin in twin pregnancy with previabile PPROM in order to achieve interval

delivery of the remaining twin, is small and has not been reproduced.³² However, in the case of abortion for previable PPRM as well as abortion of a twin unaffected by chorioamnionitis, additional non-therapeutic effects need consideration and discussion for informed consent. Abortion for previable PPRM is performed anticipating previable delivery or pulmonary hypoplasia and perinatal death. Inducing abortion for diamniotic twins if a presenting twin is affected has the added effect of losing the unaffected fetus.

Few obstetricians currently offer induction of labor for the purposes of comfort care or attempted resuscitation in periviable PPRM regardless of infection status.³³

Ending Pregnancy with Induction of Labor

It is important to recognize that the treatment for chorioamnionitis is ending the pregnancy, regardless of whether the fetus is born alive or born dead. In induced abortion, “the intention is that the fetus should not survive and that the process of abortion should achieve this.”³⁴ Thus, induced abortion achieves two effects (it ends the pregnancy to treat chorioamnionitis, and ends the life of the fetal organism). In many circumstances, the physician may be able to select separation procedures which accomplish the medically indicated purpose of separating the mother and the fetus without the secondary effect of producing a dead fetus.

Live birth, or stillbirth with the fetal corpus intact, under these circumstances of need for emergent separation is the preferable outcome over dismemberment. An intact fetal corpus, whether alive or dead, allows for parental grieving and end of life rituals acknowledging the place and meaning of the baby in the social environment of the mother and family. Experience in perinatal hospice suggests that psychological outcomes may be better for families who are allowed to begin the grieving process by holding their child’s body and performing cultural grieving rituals.³⁵⁻³⁹

The single effect of completion of parturition can be achieved with previable induction of labor. This is most expediently accomplished with vaginal misoprostol or high-dose oxytocin.^{40,41} A loading dose of 600 micrograms (mcg) of misoprostol (per vagina) followed by 200 mcg doses (per vagina) every 6 hours led to delivery within 24 hours in 80% of women; vaginal misoprostol was more successful than sublingual.^{42,43}

This obtains the indicated effect—separation of mother and fetus—and the chorioamnionitis will be appropriately treated. This method may avoid the unnecessary earlier death of the fetus and in the large majority of cases, effect separation within 24 hours. This method of rapid induction will, in most cases, be adequate to avoid serious maternal morbidity when combined with broad-spectrum antibiotics, antipyretics, close monitoring and fluid resuscitation.

In addition, rapid induction will avoid the surgical risks of dismemberment abortion, including perforation of the uterus by surgical instruments or fetal bones. There is a large meta-analysis suggesting that second trimester instrumental cervical dilation increases risks of subsequent preterm birth,⁴⁴ but other studies find conflicting results or suggesting risk depends on interval to next pregnancy.^{45,46} In addition, avoiding surgical curettage may decrease the risk of subsequent Asherman’s syndrome, since

blind dilation and curettage for any reason confers an odds ratio of 4.86 for Asherman's syndrome above the general population, an approximate 1% incidence of all D&Cs.^{47,48}

The Principle of Double Effect

Importantly, a physician who views the fetus as a second patient or even as an organism whose integrity should be respected, legitimately questions whether there is any true difference between surgical abortion and induction of labor, apart from dismemberment that might be associated with dilation and evacuation. An ethical principle called the principle of double effect can illuminate the difference.

The principle of double effect is a way of judging the acceptability of acts with good and bad effects. For an act with a bad effect to be morally acceptable, it must conform to the four criteria laid out in Table 3.

Table 3. The Principle of Double Effect
<p>Actions leading to undesirable secondary effects, even if anticipated, can be permissible when all of the following criteria are met:</p> <ol style="list-style-type: none"> 1. The primary act must be inherently good, or at least morally neutral. 2. The good effect must not be obtained by means of the bad effect. 3. The bad effect must not be intended, only permitted. 4. There must be no other means to obtain the good effect. 5. There must be a proportionately grave reason for permitting the bad effect.
Excerpt from "Double Effect Ethics Statement," used with permission from the Christian Medical and Dental Association.

In the case of chorioamnionitis in the setting of previable PPROM, the act of inducing labor is morally neutral. Every pregnancy ends in the separation of mother and fetus (except in the case of maternal death during pregnancy). Second, the good effect (i.e. preserving the mother's life from serious morbidity such as ICU admission, hysterectomy, hemorrhage, and death) must be the only effect intended, meaning that the maternal patient and the physician must keep in mind that the goal of the induction is to treat chorioamnionitis, not to kill the fetus. Third, "since the early induction of labor does not target the fetus, but the evacuation of the pathological tissues, the death of the fetus is not a means to achieve the health of the mother."⁴⁹ Fourth, the preservation of the mother's life is proportionate to the expected but undesired bad effect, the end of the fetus' life.

Clinical Considerations and Recommendations

Q. How should women diagnosed with previable PPRM be counseled?

They should be offered a realistic expectation of their pregnancy ending spontaneously or of latency and later delivery complicated almost certainly by pulmonary hypoplasia. When possible, this counseling should be offered in conjunction with a neonatologist so that the patient may better understand the guarded prognosis for the fetus. Stratifying expected neonatal outcomes based on amniotic fluid volume may be clinically useful.⁵⁰

Q. Does amnioinfusion improve outcomes over expectant management?

It is unclear whether amnioinfusion improves outcomes, and this intervention should be considered experimental.⁵¹

Summary of Recommendations and Conclusion

The following recommendations are based on good and consistent scientific evidence (Level A):

1. Criteria for chorioamnionitis and related disorders is evolving and clinicians should stay up to date on the evidence supporting terminology and treatment modalities.
2. Women with previable PPRM should be offered realistic counseling from a multidisciplinary approach

The following recommendations are based on limited and inconsistent scientific evidence (Level B):

1. Amnioinfusion is not clearly beneficial over expectant management

The following recommendations are based primarily on consensus and expert opinion (Level C):

1. Necessary separation of the mother and the fetus in order to preserve the life of the mother should prioritize delivery methods which result in a living fetus if possible, with appropriate neonatal resuscitation available.
2. In cases where delivery of a living fetus is not possible, priority should be given to delivery methods which result in an intact fetal corpus.
3. Physicians should prefer induction of labor with misoprostol to midtrimester induced abortion with mifepristone/misoprostol or dilation and evacuation.

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