



APEC Guidelines Premature Rupture of Membranes

Term PROM

Term premature rupture of membranes (PROM) is defined as rupture of membranes before the onset of labor. The most significant maternal risk of term PROM is intrauterine infection which increases with the duration of membrane rupture. Fetal risks include umbilical cord compression and ascending infection.

Preterm PROM

Preterm birth is defined as delivery before 37 weeks gestation. Prematurity is the leading cause of perinatal mortality in the US and is the major reason why we lag behind other developed nations in infant mortality rates. Approximately 70% of neonatal deaths, 36% of infant deaths, and 25-50% of cases of long-term neurologic impairment in children can be attributed to preterm birth.(ACOG, 2012) The estimated cost of preterm births exceeds \$26.2 billion annually with an average cost of care for a preterm birth ten times greater than that of a full term birth, \$32,325 to \$3,325 respectively. (CDC, 2008) In 2010, preterm birth occurred in 12.0% of 4 million births in the US and 15.6% of 58,000 births in the state of Alabama. (Hamilton, 2011)While the preterm birth rate has declined over the past 4 years (17.1% in 2006 to 15.6% in 2010), Alabama has the second highest preterm birth rate in the nation. (Hamilton, 2011)

Preterm premature rupture of membranes (pPROM) is defined as rupture of membranes before 37 weeks GA; pPROM is a complication of approximately 1/3 of all preterm births. (Mercer, 2010)Birth within 1 week is the most likely outcome for any patient with pPROM in the absence of adjunctive treatments. The earlier in gestation pPROM occurs, the longer the latency period (time between PROM and delivery). Outcomes of survivors of preterm PROM depend on GA, presence of infection, length of latency, and other maternal and fetal complications. Factors contributing to preterm PROM include:

- Intraamniotic infection
- Low socioeconomic status
- Smoking
- Low BMI <19.8
- Prior history of PROM
- Cervical insufficiency
- History of subchorionic bleeding/hematoma

Diagnosis

PROM is diagnosed by the occurrence of any 2 of the following:

- Pooling of fluid in the vaginal vault
- Positive Nitrazine test
- Ferning of vaginal fluid

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Or any 1 of the following:

- Indigo carmine pooling in the vagina after amnioinfusion
- Visible leakage of amniotic fluid from the cervix
- Biochemical test for rupture of membranes accompanied by a history consistent with SROM; several commercially available biochemical tests are on the market.
 - These biochemical tests have a specificity that ranges from 78-98% in studies. Therefore, results should be interpreted in light of the clinical history, presentation, and findings. Especially in preterm patients, ancillary information (e.g. ultrasound diagnosis of oligohydramnios) should support the diagnosis of ruptured membranes prior to enacting a management plan.
 - Furthermore, these biochemical tests add to the cost of evaluation and therefore should ideally only be utilized when the diagnosis of ruptured membranes is equivocal.
 - Clinicians who utilize these tests should familiarize themselves with the sensitivity and specificity of the particular utilized at their facility.

Management

Management depends on the GA at the time of confirmation of the diagnosis of ruptured membranes. At all gestational ages, expectant management is associated with a risk of ascending infection and umbilical cord compression, therefore the risks of expectant management must be balanced against the risks of immediate delivery. Approximately 50% of women who present with PROM will deliver in the first 7 days, many of them in the first 48 hours; however antibiotic treatment has been shown to significantly prolong latency in the setting of pPROM.

Gestational Age	Management
Term (37 weeks or more)	<ul style="list-style-type: none"> ● Proceed to delivery with route based on usual indications. ● GBS prophylaxis as indicated based on culture or CDC risk stratification if culture data unavailable.
Near term (34 to 36 weeks)	<ul style="list-style-type: none"> ● Same as for term after assessment of appropriate level of neonatal care available at facility.
Preterm (32 to 33 weeks)	<ul style="list-style-type: none"> ● Expectant management, unless fetal lung maturity is documented. ● Avoid digital cervical exams unless in active labor. ● GBS prophylaxis as indicated based on culture or CDC risk stratification if culture data unavailable. ● Antenatal corticosteroids. ● Antibiotics for latency (see regimens below). ● Delivery at level II or III nursery as appropriate.
Preterm (23 to 31 weeks)	<ul style="list-style-type: none"> ● Expectant management. ● Avoid digital cervical exams unless in active labor.

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	<ul style="list-style-type: none">• GBS prophylaxis as indicated based on culture or CDC risk stratification if culture data unavailable.• Antenatal corticosteroids.• Antibiotics for latency (see regimens below).• Delivery at level III nursery.• Magnesium sulfate infusion for neuroprotection.
Less than 23 weeks	<ul style="list-style-type: none">• Patient counseling and consultation with MFM specialist.• Expectant management or induction of labor.• Avoid digital cervical exams unless in active labor.

Recommendations

Delivery Management

- PROM at term (≥ 37 weeks) should be delivered to reduce the risk of chorioamnionitis and fetal infection.
- Delivery is also recommended when PROM occurs at 34-36 weeks of gestation.
- Delivery at 32-33 weeks with PROM may be considered if fetal pulmonary maturity has been documented.
- PROM prior to 32 weeks should be managed expectantly until 34 weeks in the absence of maternal or fetal contraindications, overt uterine infections, or fetal compromise. At 34 wk 0 d, the risk of continued expectant management begins to exceed the risk of prematurity and delivery.
- Previaible PROM < 23 weeks
Patients who develop PROM less than 23 weeks are at markedly increased risk of neonatal morbidity and mortality from extreme prematurity and, especially with PROM prior to 20 weeks, lethal fetal/neonatal pulmonary hypoplasia, as well as maternal morbidity due to chorioamnionitis and sepsis. These patients should be referred to a tertiary center for counseling and management. If there is no evidence of labor, vaginal bleeding, or infection at the time of the initial presentation, the patient may be sent home with antibiotics to prolong latency and instructions for careful temperature surveillance and follow-up while awaiting outpatient evaluation at the tertiary center. Hospitalization in a tertiary care center should be considered at 24 weeks.

Non-Delivery Management

- Patients with PROM <34 weeks, should be transported to a facility with a Level III nursery because of the potential for rapid labor progress and/or the need for expeditious delivery.
- All women with PROM and a viable fetus should receive GBS prophylaxis at the time of presentation and at the time of labor unless recent cultures (within 5 weeks) are negative for GBS. See APEC Protocol 10: Group B Streptococci. Some clinicians chose to obtain a GBS culture at the time of presentation with PROM. If this is done, these results, once available, should guide further decisions regarding GBS prophylaxis.
- Women with preterm PROM before 32 weeks who are thought to be at risk of imminent delivery should be considered candidates for fetal neuroprotective treatment with IV magnesium sulfate.(ACOG, 2013) See APEC Protocol 11: MgSO4 for Fetal Neuroprotection.
- Women with PROM between 23-33 weeks gestation should receive a single course of antenatal

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corticosteroids. Data supporting a beneficial effect of steroids at 32-33 weeks in the setting of PROM are weak, but administration can be considered in keeping with the potential benefit seen in the setting of intact membranes and this has been recently recommended by ACOG. (ACOG, 2013) For this reason, administration of antenatal corticosteroids should be given to all women with PROM less than 34 weeks.

- **Latency Antibiotic Regimens**

- Multiple studies have documented the ability of antibiotic therapy to prolong pregnancy and reduce infection in the setting of expectant management of PROM remote from term.
- **All patients with PROM should receive latency antibiotics regardless of GBS antibiotics.**
- The most well studied regimen was that used in the NICHD Maternal-Fetal Medicine Units Network trial: A 48-hour course of intravenous **ampicillin (2 g IV q 6) and erythromycin (250 mg IV q 6) followed by 5 days of amoxicillin (250 mg po q 8) and erythromycin (333 mg po q 8).** ACOG currently endorses a combination of erythromycin and ampicillin or amoxicillin for 7 days, (ACOG, 2013) however, because of the side effects associated with this regimen and other studies suggesting benefit from slightly longer latency regimens, a number of alternative regimens have been developed. The key elements are: 1) a broad spectrum beta-lactam type antibiotic with gram negative coverage and 2) a macrolide antibiotic with coverage for atypical organisms.
- At UAB and USA, the standard regimen for PROM is: **Ampicillin 2 g IV q 6** while in Labor and Delivery followed by **Amoxicillin 500mg po TID x 10 days.** In addition, patients receive **Azithromycin 1 gram po on day of admission and day 5.**
- For patients who are PCN allergic, oral cephalexin 500 mg TID can be considered; prolonged oral clindamycin is NOT recommended due to GI side effects
- **Latency antibiotics should be continued until the onset of labor or until 10 days of therapy have been completed. Regardless of when labor ensues, GBS prophylaxis should be provided during labor unless a recent culture documented negative results.**

Assessment

- Assess GA, fetal presentation, and well-being in all patients with PROM. Patients with intrauterine infection, abruptio placentae, or fetal compromise should be expeditiously delivered.
- Digital cervical examinations increase the risk of infection and should be avoided unless the patient is in active labor or delivery is imminently planned. Sterile speculum examination provides an opportunity to inspect for cervicitis and umbilical cord prolapse, assess cervical dilatation and effacement, and obtain cultures as appropriate.

Transport to tertiary facility

In order to maximize perinatal outcomes, delivery of preterm infants should occur at facilities capable of providing the appropriate level of neonatal resuscitative and supportive care commensurate with the gestational age. The American Academy of Pediatrics has recently redefined levels of neonatal care providing recommendations to ensure each newborn infant if delivered and cared for in a facility

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most appropriate for his or her needs, see Table 1: Levels of Neonatal Care. (Pediatrics, 2012) The importance of delivery location is underscored by the improved survival of these neonates when delivered at tertiary care centers. (Cunningham et al., 2010)

Quality Indicators/Benchmarks

- Antenatal corticosteroids <34 weeks GA
- Antibiotics for latency
- Magnesium sulfate for fetal neuroprotection <32 weeks GA
- Delivery at appropriate facility

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Table 1: Levels of Neonatal Care

Level of Care	Capabilities	Health Care Provider Types
Level I Well newborn nursery	<ul style="list-style-type: none"> • Provide neonatal resuscitation at every delivery • Evaluate and provide postnatal care to stable term newborn infants • Stabilize and provide care for infants born 35-37 weeks GA who remain physiologically stable • Stabilize newborn infants who are ill and those born at < 35 wks gestation until transfer to a higher level of care 	<ul style="list-style-type: none"> • Pediatricians, family physicians, nurse practitioners, and other advanced practice registered nurses
Level II Special care nursery	<p>Level I capabilities plus:</p> <ul style="list-style-type: none"> • Provide care for infants born \geq 32 wks GA and weighing \geq 1500 g who have physiologic immaturity or who are moderately ill with problems that are expected to resolve rapidly and are not anticipated to need subspecialty services on an urgent basis • Provide care for infants convalescing after intensive care • Provide mechanical ventilation for brief duration (<24 h) or continuous positive airway pressure or both • Stabilize infants born before 32 wk gestation and weighing < 1500 g until transfer to a neonatal intensive care facility 	<ul style="list-style-type: none"> • Level I health care providers plus: Pediatric hospitalists, neonatologists, and neonatal nurse practitioners
Level III NICU	<p>Level II capabilities plus:</p> <ul style="list-style-type: none"> • Provide sustained life support • Provide comprehensive care for infants born < 32 wks GA and weighing < 1500 g and born at all GA and birth weights with critical illness • Provide prompt and readily available access to a full range of pediatric medical subspecialists, and pediatric ophthalmologists • Provide a full range of respiratory support that may include conventional and/or high-frequency ventilation and inhaled nitric oxide • Perform advanced imaging, with interpretation on an urgent basis, including computed tomography, MRI, and echocardiography 	<ul style="list-style-type: none"> • Level II health care providers plus: Pediatric medical subspecialists, pediatric anesthesiologists, pediatric surgeons, and pediatric ophthalmologists
Level IV Regional NICU	<p>Level III capabilities plus:</p> <ul style="list-style-type: none"> • Located within an institution with the capability to provide surgical repair of complex congenital or acquired conditions • Maintain a full range of pediatric medical subspecialists, pediatric surgical subspecialists, and pediatric anesthesiologists at the site • Facilitate transport and provide outreach education 	<ul style="list-style-type: none"> • Level III health care providers plus: Pediatric surgical subspecialists

(Pediatrics, 2012)

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