Chapter 6
Premature Rupture of Membranes and Preterm Labor

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Introduction

Premature rupture of membranes (PROM) and preterm labor are challenging obstetric complications for any emergency physician. In the United States, preterm delivery complicates approximately one in ten births and is the cause of at least 75% of neonatal deaths, not including congenital malformations. When preterm premature rupture of membranes occurs, several complications can occur including infection, premature delivery, placental abruption, and umbilical cord prolapse.

Complications of late pregnancy including PROM and preterm labor are infrequently managed in the emergency department (ED). Many hospitals have protocols where these patients are triaged directly to a labor and delivery (L&D) unit for further management by an obstetrician. However, an obstetrician or L&D unit may not always be immediately available and emergency physicians must be comfortable initially managing these complications. The rate of fetal and maternal morbidity can be reduced with accurate diagnosis of PROM and preterm labor, intervention to delay preterm delivery, timely administration of corticosteroids, and in certain cases, magnesium sulfate and antibiotics.

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J. Borhart (ed.), *Emergency Department Management of Obstetric Complications*,
DOI 10.1007/978-3-319-54410-6_6

Preterm Premature Rupture of Membranes

Premature rupture of membranes (PROM) is rupture of membranes before labor. Preterm PROM refers to the rupture of membrane before labor that occurs prior to 37 weeks of gestation. Preterm PROM complicates approximately 3% of all pregnancies in the United States [1]. During pregnancy, the amniotic membrane protects the fetus from infection while providing an environment that allows for both growth and movement. Fluid exchange is facilitated in part by fetal swallowing and urination. The fetal airway contains a secreted fluid that allows for fetal breathing and promotes respiratory development.

Membrane rupture may occur for several reasons. At term it occurs due to normal physiologic weakening of membranes, while preterm membrane rupture can occur for several pathologic conditions [2, 3]. At earlier gestational age, one of the most common reasons is intraamniotic infection [4]. A previous history of preterm PROM is a risk factor for either preterm PROM or preterm labor in future pregnancies. Other risk factors include short cervical length, history of vaginal bleeding during pregnancy, low socioeconomic status, cigarette smoking, and illicit drug use [5, 6]. Other cases may be without any identifiable risk factors.

Labor is the ideal result of ruptured membranes at term; however, when the fetus is preterm, labor that often follows membrane rupture is problematic given the associated fetal complications of prematurity.

Emergency Department Evaluation

Initial evaluation of the patient presenting with preterm PROM includes determination of duration, amount, and persistence of fluid leakage. Classically, patients report a sudden gush of fluid with continuous leakage. If the clinical history is unclear, patients should be asked questions about recent vaginal or cervical infections, recent sexual activity, douching, and previous pelvic surgery.

The next step in diagnosis is determining the gestational age of the pregnancy based on patient's reported last menstrual period (LMP) or previous ultrasonography scans. If the patient is unable to report either menstrual or ultrasound dating, an ultrasound can be obtained in the emergency department to determine gestational age. Ultrasounds become less accurate for obstetric dating with advancing gestational age. As a general rule, ultrasound dating has an accuracy of +/− 2 weeks in the second trimester and +/− 3 weeks in the third trimester [7]. In addition to estimating gestational age, obstetric ultrasound is indicated in order to determine the fetal presentation, an estimated fetal weight, and amount of amniotic fluid. Oligohydramnios, defined as amniotic fluid index (AFI) ≤5 cm, may be present in PROM, but is not diagnostic.

Examination of patients with possible PROM should be performed under sterile conditions with a sterile speculum to minimize the risk of introduction of infection.

Table 6.1 Testing for PROM

Method	Result
Nitrazine	Amniotic fluid pH 7.1–7.3 turns nitrazine paper yellow; >7.3 is blue
Ferning	Amniotic fluid crystallizes and appears like a fern, identified under microscope
Pooling on speculum exam	Amniotic fluid collects in the posterior vaginal vault
Ultrasonography (not diagnostic)	Oligohydramnios (defined as AFI <5)

Avoid direct digital examination of the cervix in women with PROM because the risk of infection has been shown to be proportional to the number of digital examinations [8]. Table 6.1 lists the components of diagnosing PROM. At speculum examination, the diagnosis is confirmed by visualization of passing of fluid from the endocervical canal into the vagina and/or a "pool" of fluid in the posterior vaginal vault. Having the patient cough or applying gentle fundal pressure may assist in visualizing the passage of fluid. If in doubt, the fluid can be tested via nitrazine test for pH. The pH of normal vaginal fluid is 4.5–6, while amniotic fluid pH is 7.1–7.3 Blood or semen contamination, alkaline antiseptics, and bacterial vaginosis can increase the vaginal pH and lead to a false-positive nitrazine test. Vaginal fluid may also be applied to a microscope slide and examined for the presence of ferning. During the speculum exam, the physician should visualize the cervix and assess for dilation and effacement and look for any presenting fetal parts or umbilical cord prolapse. Cultures for group B streptococcus, chlamydia, and gonorrhea can also be collected during the speculum examination.

Management

Once the diagnosis of PROM is established, the management depends on the gestational age and maturity of the fetus. Important factors include whether or not labor is present and if there is suspected intraamniotic infection. All patients with preterm PROM should be evaluated for intraamniotic infection (chorioamnionitis). Chorioamnionitis occurs when vaginal or cervical bacteria ascend into the amniotic cavity and initiate an inflammation of the chorion and amnion. Risk factors include prolonged labor, PROM, and excessive digital examinations. Chorioamnionitis occurs in 15–25% of women with preterm PROM [9]. The incidence of infection is higher with earlier gestational age [4]. Table 6.2 lists diagnostic criteria for chorioamnionitis

The management of preterm PROM includes administration of antibiotics to reduce neonatal and maternal infections and to prolong the latency period (time from membrane rupture to delivery). There are several antibiotic regimens that have shown benefit. The regimen described by the American College of Obstetricians and Gynecologists (ACOG) in a 2016 practice bulletin is a 7-day antibiotic course

Table 6.2 Diagnosis of chorioamnionitis (typically fever plus two other signs)

Maternal signs and symptoms
Fever (>100.4 °F)
Tachycardia (>100/min)
Malodorous vaginal discharge
Fundal tenderness
Leukocytosis
Fetal signs
Fetal tachycardia (>160/min)
Decreases in variability on fetal heart rate monitoring

starting with intravenous ampicillin (2 g every 6 h) and oral erythromycin (250 mg every 6 h) for 48 h, followed by oral amoxicillin (250 mg every 8 h) and erythromycin base (333 mg every 8 h) [10]. Intrapartum antibiotic prophylaxis against group B streptococcus is also indicated for women with preterm PROM at risk for preterm delivery whose carrier status is unknown.

With regards to fetal lung maturity, a fetus beyond 36 weeks is very likely to have reached lung maturity. In a fetus before 36 weeks, administration of corticosteroids can accelerate lung maturity. Corticosteroids have the additional benefits of reducing neonatal mortality, respiratory distress syndrome, intraventricular hemorrhage, and necrotizing enterocolitis [11–13]. Previous studies have suggested increased risk of infection with administration of corticosteroids in the setting of preterm PROM, but larger studies have not supported these findings. A common regimen is intramuscular betamethasone 12 mg every 24 h for 2 days [14]. Completion of one course of corticosteroids is indicated, irrespective of membrane status, for pregnant women between 24 0/7 weeks and 34 0/7 weeks if there is a concern for premature delivery within 7 days [15].

Complications

Complications associated with preterm PROM include active preterm labor with malpresentation of fetus (breech presentation being the most common), umbilical cord prolapse, infection, fetal distress, and placental abruption (2–5% of pregnancies) [16]. After preterm PROM, infection and umbilical cord accidents contribute to 1–2% of fetal demise [17]. The most significant risks to the fetus after preterm PROM are the myriad of complications of prematurity, the most common being respiratory distress. Additionally, preterm PROM with intrauterine inflammation has been associated with increased risk of impaired neurodevelopment [18]. In approximately 50% of preterm PROM, birth will occur within 1 week [10]. Latency after membrane rupture is inversely correlated to gestational age at rupture of membranes. Obstetric consultation should be obtained early in the ED course of a patient with PROM or preterm PROM. Once fetal viability has been reached (>23 weeks), hospitalization is recommended for patients with PROM and preterm PROM.

Preterm Labor

Preterm birth is the leading cause of neonatal mortality and one of the most common reasons for hospitalization [19]. In the United States, approximately 12% of all births occur before term, and preterm labor preceded about 50% of these births [20, 21]. Preterm birth accounts for 70% of neonatal deaths and 36% of infant deaths as well as 25–50% of long-term neurologic impairment in children [22].

Preterm birth is defined as birth between 20 0/7 weeks of gestation and 36 6/7 weeks of gestation. In order to more accurately describe deliveries that occur at or beyond 37 0/7 weeks, new obstetric guidelines have more clearly designated early term as 37 to 38 6/7 weeks and full term as 39 0/7 weeks of gestation through 40 6/7 weeks of gestation [23]. The risk of poor birth outcomes generally decreases with advancing gestational age. The risk is highest for infants born before 34 weeks; however, even infants born between 34 and 37 weeks are more likely to have delivery complications, long-term impairment, and early death than those born later in pregnancy [19]. The risks of perinatal, neonatal, and infant morbidity and mortality are lowest for infants born between 39 0/7 weeks of gestation and 40 6/7 weeks of gestation [24, 25]. Spontaneous preterm birth includes birth that follows preterm labor, preterm PROM, and cervical insufficiency, but does not include indicated preterm delivery for either maternal or fetal condition.

Risk Factors

Identifying women who will give birth preterm is an inexact process and can be very challenging as the causes of preterm birth are not well understood. One of the biggest risk factors for preterm birth is a prior preterm birth, which increases a woman's risk by about twofold [23]. Another risk factor is short cervical length as measured by transvaginal ultrasound [26]. In most studies this is defined by cervix less than 2.5 cm up to 24 weeks gestational age, and in some studies up to 28 weeks [27]. Other risk factors for preterm birth include demographic factors, current pregnancy complications, substance abuse, uterine anomalies, iatrogenic complications, infections, and psychosocial stressors (Table 6.3). Additionally, some studies have linked previous uterine or cervical instrumentation to preterm labor.

Diagnosis

The diagnosis of preterm labor is usually based on clinical criteria of regular contractions accompanied by cervical dilation, effacement, or both before 37 weeks of gestation. It can also be defined by initial presentation of regular contractions and cervical dilation of at least 2 cm. Less than 10% of women who present with these

Table 6.3 Risk factors for preterm birth

Demographic:
Extremes of age (>40 or teenager)
Low socioeconomic status
Substance abuse (tobacco, cocaine)
Psychosocial stressors
Reproductive:
Prior preterm delivery
Uterine anomalies
Cervical incompetence
Placental abruption
Vaginal bleeding in pregnancy
Infectious:
Urinary tract infections
Non-uterine infections
Vaginal infections (bacterial vaginosis)

clinical findings actually give birth within 7 days of presentation [28]. Some of the early maternal signs of preterm labor include increase or change in vaginal discharge, pain from uterine contractions (sometimes reported as lower back pain), pelvic pressure, vaginal bleeding, and leakage of fluid.

Once cervical change and uterine contractions are present, the determination of prematurity is based on patient's reported LMP or gestational age determined by prior ultrasound. If there was no prenatal care, an ED ultrasound may assist in obtaining an estimated gestational age. In general, a fetus measuring less than 2500 grams on ultrasound is likely to be premature. To differentiate false labor (Braxton Hicks contractions) from true labor, uterine contraction monitoring and repeat cervical exam are used.

Management of Preterm Labor

The initial ED evaluation of a woman with possible premature labor includes urinalysis, complete blood count, type and screen, and ultrasonography. If delivery is not imminent, and an L&D unit is immediately available, these can be completed once the patient is transported. Intravenous hydration with 1–2 L of Lactated Ringers may assist with resolution of irregular contractions, although it is not an effective treatment for true preterm labor. Bed rest is indicated until diagnosis is clear. Additionally, any underlying causes for preterm contractions such as urinary tract infections should be treated.

The management of preterm labor hinges on the gestational age of the fetus and stability of the mother. If the fetus is viable and the mother is stable, the goal is to prolong pregnancy for up to 48 h to allow for corticosteroid treatment and safe transfer of the patient. This is accomplished with the use of tocolytics [29].

Tocolytics may be initiated in the ED in close consultation with an obstetrician to attempt to halt preterm labor

Several tocolytic agents have been used to inhibit contractions, and beta-adrenergic receptor agonists, calcium channel blockers, and nonsteroidal anti-inflammatory drugs (NSAIDs) are all considered first-line medications [30, 31]. Two of the most commonly used are nifedipine (calcium channel blocker) and indomethacin (NSAID). Because of potential maternal complications, beta-adrenergic receptor agonists and calcium channel blockers should be used with caution in combination with magnesium sulfate. Antenatal indomethacin has been associated with fetal necrotizing enterocolitis in some studies.

Only women with fetuses that would benefit from a 48-h delay in delivery should receive tocolytic treatment. Women with contractions but without cervical change should not be treated with tocolytics, and tocolytics are generally not indicated before fetal viability. Other contraindications include maternal or fetal distress, eclampsia, and preterm PROM (Table 6.4). The upper limit of tocolytic use is 34 weeks.

Magnesium sulfate was previously administered as a tocolytic, but now it is used mostly for fetal neuroprotection if birth is anticipated before 32 weeks. Clinical trials of magnesium sulfate for neuroprotection suggest that the predelivery administration reduces the occurrence of cerebral palsy [32]. None of the trials demonstrated significant prolongation of pregnancy when magnesium sulfate was given for neuroprotection. Hospitals that elect to use magnesium sulfate usually have protocols for its usage including administration regimen, concurrent tocolysis, and monitoring.

The single most beneficial intervention for improvement of neonatal outcomes among preterm births is antenatal corticosteroids. A single course is recommended for women between 24 0/7 weeks and 34 0/7 weeks of gestation and may be considered for pregnant women starting at 23 weeks who are at risk of delivery within 7 days. Corticosteroids are considered routine for all preterm deliveries because of the associated decreased neonatal morbidity and mortality [11, 33]. Neonates that receive corticosteroids have lower rates of respiratory distress syndrome, intracranial hemorrhage, necrotizing enterocolitis, and death.

A single repeat course of antenatal corticosteroids should be considered in women whose prior course was at least 7 days previously and who remain at risk for delivery at less than 34 weeks. A recent randomized controlled trial has suggested benefit in corticosteroids from 34–37 weeks in setting of late preterm birth [34]. The decision to give corticosteroids should be made in consultation with an obstetrician.

Table 6.4 Contraindications to tocolysis

Intrauterine fetal demise
Lethal fetal anomaly
Nonreassuring fetal status
Severe preeclampsia or eclampsia
Maternal bleeding with hemodynamic instability
Chorioamnionitis
Maternal contraindication

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The most commonly used corticosteroids are betamethasone and dexamethasone. The treatment for a primary or rescue course should consist of either two 12-mg dose of betamethasone given intramuscularly 24 h apart or four 6-mg doses of dexamethasone every 12 h administered intramuscularly [35]. The first dose should be given even if delivery is likely before the second dose can be administered, as there is evidence showing benefit of even a single dose.

Antibiotics and Preterm Labor

Several maternal infections have been associated with preterm labor. Most studies have failed to demonstrate that antibiotics have any benefit of preventing preterm birth, respiratory distress syndrome, or neonatal sepsis. Nevertheless, maternal infections identified in the ED should be treated. This is distinct from using antibiotics for preterm PROM and group B streptococci carriers [36, 37]. If the group B streptococci status of a woman is unknown and delivery is anticipated, antibiotics to prevent group B streptococcus in the neonate should be initiated. Penicillin remains the drug of choice and ampicillin is an acceptable alternative. Erythromycin is no longer recommended due to resistance. If there is severe allergic reaction to penicillin (anaphylaxis), cefazolin may be administered. All antibiotics for group B streptococcus prophylaxis should be given intravenously [37].

Disposition

In many cases, patients presenting to the ED in preterm labor can be safely transported to a L&D unit for further management by an obstetrician. Because of the high risk associated with delivery outside an obstetric unit, the emergency physician should make every effort to arrange transport to a facility with both obstetric and neonatal resources if time allows. In the setting of preterm birth, the infant may require intensive care services immediately after delivery. Obstetric consultation should be sought early in the ED course of any patient in preterm labor. Some births are precipitous, and an obstetrician or L&D unit may not be immediately available. Emergency physicians must be prepared to deliver a premature infant and resuscitate mother and baby as necessary.

Summary

Preterm delivery occurs in approximately 12% of all births in the United States and contributes to significant perinatal morbidity and mortality. Preterm PROM can complicate a portion of the preterm deliveries. Diagnosis of preterm labor and preterm PROM can be initiated in the emergency department in consultation with an

obstetrician. In all patients with preterm PROM, gestational age, fetal presentation, and fetal well-being should be determined. The emergency physician should evaluate for intrauterine infection, placental abruption, and fetal compromise.

Almost all cases of preterm PROM, PROM, and preterm labor will warrant admission to an obstetrics unit. The ultimate obstetric management depends on gestational age and risks of delivery versus risks of expectant management. Corticosteroids are recommended for pregnant women with anticipated preterm delivery and tocolytic treatment can be used for short-term prolongation of pregnancy (up to 48 h). In cases of imminent delivery, determination of fetal position is of utmost importance. Intravenous magnesium sulfate is recommended to reduce the severity and risk of cerebral palsy in infants if administered when birth is anticipated before 32 weeks. If delivery is anticipated and the group B streptococcus status is unknown, antibiotics should be initiated for prophylaxis.

Key Points

- Speculum exam to rule out PROM should be done under sterile technique.
- Direct digital examination should be avoided in PROM unless delivery seems imminent.
- The single most beneficial intervention for improvement of neonatal outcomes among preterm births is antenatal corticosteroids.
- A single course of corticosteroids are recommended for women between 24 0/7 and 34 0/7 weeks gestational age who are at risk for preterm delivery within 7 days.
- Magnesium sulfate is used for fetal neuroprotection if birth is anticipated before 32 0/7 weeks and reduces the risk of cerebral palsy in infants. Tocolytics can be used for up to 48 h to allow for corticosteroids
- A 7-day course of antibiotic therapy is indicated in women with preterm PROM less than 34 0/7 weeks.

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