INTERIM UPDATE

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INTERIM UPDATE: This Practice Bulletin is updated to reflect a limited, focused change to clarify that antenatal corticosteroids should be administered when a woman is at risk of preterm delivery within 7 days.

Premature Rupture of Membranes

Preterm delivery occurs in approximately 12% of all births in the United States and is a major factor that contributes to perinatal morbidity and mortality (1, 2). Preterm premature rupture of membranes (PROM) complicates approximately 3% of all pregnancies in the United States (3). The optimal approach to clinical assessment and treatment of women with term and preterm PROM remains controversial. Management hinges on knowledge of gestational age and evaluation of the relative risks of delivery versus the risks of expectant management (eg, infection, abruptio placentae, and umbilical cord accident). The purpose of this document is to review the current understanding of this condition and to provide management guidelines that have been validated by appropriately conducted outcome-based research when available. Additional guidelines on the basis of consensus and expert opinion also are presented.

Background

The definition of *PROM* is rupture of membranes before the onset of labor. Membrane rupture before labor and before 37 weeks of gestation is referred to as preterm PROM. Management is influenced by gestational age and the presence of complicating factors, such as clinical infection, abruptio placentae, labor, or nonreassuring fetal status. An accurate assessment of gestational age and knowledge of the maternal, fetal, and neonatal risks are essential to appropriate evaluation, counseling, and care of patients with PROM.

Etiology of Premature Rupture of Membranes

Membrane rupture may occur for a variety of reasons. Although membrane rupture at term can result from a normal physiologic weakening of the membranes combined with shearing forces created by uterine contractions, preterm PROM can result from a wide array of pathologic mechanisms that act individually or in concert (4, 5). Intraamniotic infection has been shown to be commonly associated with preterm PROM, especially at earlier gestational ages (6). A history of preterm PROM is a major risk factor for preterm PROM or preterm labor in a subsequent pregnancy (7, 8). Additional risk factors associated with preterm PROM are similar to those associated with spontaneous preterm birth and include short cervical length, second-trimester and third-trimester bleeding, low body mass index, low socioeconomic status, cigarette smoking, and illicit drug use (9–12). Although each of these risk factors is associated with preterm PROM, it often occurs in the absence of recognized risk factors or an obvious cause.

Term Premature Rupture of Membranes

At term, PROM complicates approximately 8% of pregnancies and generally is followed by the prompt onset of spontaneous labor and delivery. In a large randomized trial, one half of women with PROM who were managed

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expectantly gave birth within 5 hours and 95% gave birth within 28 hours of membrane rupture (13). The most significant maternal consequence of term PROM is intrauterine infection, the risk of which increases with the duration of membrane rupture.

Preterm Premature Rupture of Membranes

Regardless of obstetric management or clinical presentation, birth within 1 week of membrane rupture occurs in at least one half of patients with preterm PROM (5). Latency after membrane rupture is inversely correlated with the gestational age at membrane rupture (14). Cessation of amniotic fluid leakage with restoration of normal amniotic fluid volume may occur in the setting of spontaneous preterm PROM and is associated with favorable outcomes (15).

Among women with preterm PROM, clinically evident intraamniotic infection occurs in approximately 15–25% (16), and postpartum infection occurs in approximately 15–20%; the incidence of infection is higher at earlier gestational ages (6, 17). Abruptio placentae complicates 2–5% of pregnancies with preterm PROM (18, 19).

The most significant risks to the fetus after preterm PROM are complications of prematurity. Respiratory distress has been reported to be the most common complication of preterm birth (20). Sepsis, intraventricular hemorrhage, and necrotizing enterocolitis also are associated with prematurity, but these are less common near to term. Preterm PROM with intrauterine inflammation has been associated with an increased risk of neurodevelopmental impairment (21, 22), and early gestational age at membrane rupture also has been associated with an increased risk of neonatal white matter damage (23). However, there are no data that suggest that immediate delivery after presentation with PROM will avert these risks. Infection and umbilical cord accident contribute to the 1–2% risk of antenatal fetal demise after preterm PROM (24).

Previable Premature Rupture of Membranes

Rupture of the membranes before viability occurs in less than 1% of pregnancies. The probability of neonatal death and morbidity associated with PROM decrease with longer latency and advancing gestational age (25). In a review of preterm PROM between 14 weeks and 24 weeks of gestation, perinatal deaths were more or less equally divided between stillbirths and neonatal deaths. Survival rates were much improved with expectant management following membrane rupture after 22 weeks of gestation compared with membrane rupture before 22 weeks of gestation (57.7% versus 14.4%, respectively) (26).

Most studies of second-trimester and previable PROM are retrospective and include only expectantly managed cases. Thus, they likely overestimate survival rates because of selection bias. Survival data may vary by institution.

Significant maternal complications that occur after previable PROM include intraamniotic infection, endometritis, abruptio placentae, and retained placenta (26). Although it occurs infrequently, life-threatening maternal infection may complicate expectant management of previable PROM. Maternal sepsis is reported in approximately 1% of cases (26), and isolated maternal deaths due to infection have been reported in this setting.

Latency periods appear to be prolonged with second-trimester preterm PROM compared with later gestational ages. However, 40–50% of patients with previable PROM will give birth within the first week and approximately 70–80% will give birth 2–5 weeks after membrane rupture (26–28).

The rate of pulmonary hypoplasia after PROM before 24 weeks of gestation varies widely among reports, but is likely in the range of 10–20%. Pulmonary hypoplasia is associated with a high risk of mortality (26), but is rarely lethal with membrane rupture subsequent to 23–24 weeks of gestation (29), presumably because alveolar growth adequate to support postnatal development already has occurred. Early gestational age at membrane rupture, and low residual amniotic fluid volume are the primary determinants of the incidence of pulmonary hypoplasia (30, 31).

Prolonged oligohydramnios also can result in fetal deformations, including Potter-like facies (eg, low-set ears and epicanthal folds) and limb contractures or other positioning abnormalities. The reported frequency of skeletal deformations varies widely (1.5–38%) but many of these resolve with postnatal growth and physical therapy (26, 32).

Clinical Considerations and Recommendations

▶ *How is premature rupture of membranes diagnosed?*

Most cases of PROM can be diagnosed on the basis of the patient's history and physical examination. Examination should be performed in a manner that minimizes the risk of introducing infection. Because digital cervical examinations increase the risk of infection and add little information to that available with speculum

examination, digital examinations generally should be avoided unless the patient appears to be in active labor or delivery seems imminent (33, 34). Sterile speculum examination provides an opportunity to inspect for cervicitis and umbilical cord prolapse or fetal prolapse, assess cervical dilatation and effacement, and obtain cultures as appropriate.

The diagnosis of membrane rupture typically is confirmed by the visualization of amniotic fluid passing from the cervical canal and pooling in the vagina; a basic pH test of vaginal fluid; or arborization (ferning) of dried vaginal fluid, which is identified under microscopic evaluation. The normal pH of vaginal secretions is generally 4.5–6.0, whereas amniotic fluid usually has a pH of 7.1–7.3. False-positive test results may occur in the presence of blood or semen, alkaline antiseptics, or bacterial vaginosis. Alternatively, false-negative test results may occur with prolonged membrane rupture and minimal residual fluid.

In equivocal cases, additional tests may aid in the diagnosis. Ultrasonographic examination of amniotic fluid volume may be a useful adjunct, but is not diagnostic. Fetal fibronectin is a sensitive but nonspecific test for ruptured membranes; a negative test result is strongly suggestive of intact membranes, but a positive test result is not diagnostic of PROM (35). Several commercially available tests for amniotic proteins are currently on the market, with high reported sensitivity for PROM (36, 37). However, false-positive test result rates of 19–30% have been reported in patients with clinically intact membranes and symptoms of labor (38, 39). These test kits should be considered ancillary to standard methods of diagnosis. If the diagnosis remains unclear after a full evaluation, membrane rupture can be diagnosed unequivocally with ultrasonographically guided transabdominal instillation of indigo carmine dye, followed by the passage of blue-dyed fluid into the vagina, which is documented by a stained tampon or pad. It is important to note that the maternal urine also will turn blue and should not be confused with amniotic fluid.

▶ *What does the initial management involve once PROM has been confirmed?*

In all patients with PROM, gestational age, fetal presentation, and fetal well-being should be determined. The examination should evaluate for evidence of intrauterine infection, abruptio placentae, and fetal compromise. If results are not already available and if an indication for treatment is not already present, culture for group B streptococci (GBS) should be obtained when expectant management is being considered.

In patients with preterm PROM, an initial period of electronic fetal heart rate monitoring and uterine activity monitoring offers the opportunity to identify abnormal fetal heart rate tracings and to evaluate for contractions (40). Management after confirmation of the diagnosis of PROM is dependent primarily on gestational age and is discussed in more detail in the following paragraphs. Nonreassuring fetal status and clinical chorioamnionitis are indications for delivery. Vaginal bleeding should raise concern for abruptio placentae and also should prompt consideration of delivery, with the decision based on fetal status, the amount of bleeding, and gestational age.

▶ *What is the optimal method of initial management for a patient with PROM at term?*

Gestational age and fetal position should be confirmed and fetal heart rate monitoring should be used to assess fetal status. Group B streptococcal prophylaxis should be given based on prior culture results or intrapartum risk factors if cultures have not been previously performed (41).

A meta-analysis of 12 randomized controlled trials (6,814 women) found that induction of labor reduced the time to delivery and the rates of chorioamnionitis, endometritis, and admission to the neonatal intensive care unit without increasing the rates of cesarean delivery or operative vaginal delivery (42). The largest of these trials also found that women viewed induction of labor more positively than expectant management (13). Induction of labor with prostaglandins has been shown to be equally effective for labor induction compared with oxytocin but is associated with higher rates of chorioamnionitis (13). Infection is also a concern with mechanical methods of cervical ripening, such as the Foley balloon, but there are insufficient data on which to base a recommendation for mechanical methods of cervical ripening in the setting of PROM. A meta-analysis of two trials suggests that use of prophylactic antibiotics may reduce infectious morbidity, but prompt induction of labor was not standard care in either study. Thus, there is insufficient evidence to justify the routine use of prophylactic antibiotics with PROM at term in the absence of an indication for GBS prophylaxis (43–45).

These meta-analysis data indicate that patients benefitted from induction of labor compared with expectant management and suggest that for women with PROM at 37 0/7 weeks of gestation or more, if spontaneous labor does not occur near the time of presentation in those who do not have contraindication to labor, labor should be induced, generally with oxytocin infusion. However, a course of expectant management may be acceptable for a patient who declines induction of

labor as long as the clinical and fetal conditions are reassuring and she is adequately counseled regarding the risks of prolonged PROM. During induction of labor with oxytocin, a sufficient period of adequate contractions (at least 12–18 hours) should be allowed for the latent phase of labor to progress before diagnosing failed induction and moving to cesarean delivery (46–48).

▶ *When is delivery recommended for the preterm fetus in the presence of premature rupture of membranes?*

Nonreassuring fetal status, clinical chorioamnionitis, and significant abruptio placentae are clear indications for delivery. Otherwise, gestational age is a primary factor when considering delivery versus expectant management (Box 1).

However, the optimal gestational age for delivery is unclear and controversial. A meta-analysis of seven randomized controlled trials, including 690 women, concluded there was insufficient evidence to guide clinical practice regarding the risks and benefits of expectant management versus delivery in the setting of preterm PROM (49). The trials were insufficiently powered, had methodological weaknesses, and were variable in the gestational ages included.

More recently, two randomized controlled trials evaluated delivery versus expectant management between 34 weeks and 37 weeks of gestation and included a total of 736 women (50, 51). Combining data from the two studies, induction of labor did not produce a statistically significant reduction in the rate of neonatal sepsis (2.7% at 34 weeks versus 4.1% at 37 weeks of gestation, relative risk [RR], 0.66; 95% confidence interval [CI], 0.3–1.5). However, induction of labor did significantly reduce the risk of chorioamnionitis (1.6% at 34 weeks versus 5.3% at 37 weeks of gestation, RR, 0.31; 95% CI, 0.1–0.8), although there were no other significant differences between the two groups. These studies did not have sufficient power to show a statistically significant reduction in the rate of neonatal sepsis because the overall rate of sepsis was lower than anticipated. These findings are consistent with other smaller, similarly designed trials (52, 53) and those conducted in women at term (13, 42).

Despite these data, the optimal gestational age for delivery remains controversial. Recently there has been a focus on the short-term (54) and long-term (55) risks associated with late preterm birth. However, the relevance of this to the management of women with ruptured membranes is unclear because neonates born from pregnancies complicated by preterm PROM have a higher rate of adverse outcomes compared with controls matched for gestational age (56). Furthermore, chorioamnionitis, prolonged membrane rupture, and oligohydramnios are risk factors for adverse neonatal outcomes with preterm PROM (56, 57).

At 34 0/7 weeks of gestation or greater, delivery is recommended for all women with ruptured membranes. If expectant management is continued beyond 34 0/7 weeks of gestation, the balance between benefit and risk should be carefully considered and discussed with the patient, and expectant management should not

Box 1. Chronologic Management of Premature Rupture of Membranes ⇦

Early Term and Term (37 0/7 weeks of gestation or more)

- Proceed to delivery
- GBS prophylaxis as indicated

Late Preterm (34 0/7–36 6/7 weeks of gestation)

- Same as for early term and term

Preterm (24 0/7–33 6/7 weeks of gestation)*†

- Expectant management
- Antibiotics recommended to prolong latency if there are no contraindications
- Single-course corticosteroids
- GBS prophylaxis as indicated

Less than 24 weeks of gestation‡§

- Patient counseling
- Expectant management or induction of labor
- Antibiotics may be considered as early as 20 0/7 weeks of gestation
- GBS prophylaxis is not recommended before viability‖
- Corticosteroids are not recommended before viability‖
- Tocolysis is not recommended before viability‖
- Magnesium sulfate for neuroprotection is not recommended before viability†‖

Abbreviation: GBS, group B streptococci.

*Unless fetal pulmonary maturity is documented.

†Magnesium sulfate for neuroprotection in accordance with one of the larger studies.

‡The combination of birth weight, gestational age, and sex provide the best estimate of chances of survival and should be considered in individual cases.

§Periviable Birth. Obstetric Care Consensus No. 3. American College of Obstetricians and Gynecologists. Obstet Gynecol 2015;126:e82–94.

‖May be considered for pregnant women as early as 23 0/7 weeks of gestation.

extend beyond 37 0/7 weeks of gestation. Patients with PROM before 34 0/7 weeks of gestation should be managed expectantly if no maternal or fetal contraindications exist (53).

▶ *What general approaches are used in cases of preterm PROM managed expectantly?*

Expectant management of preterm PROM generally consists of hospital admission with periodic assessment for infection, abruptio placentae, umbilical cord compression, fetal well-being, and labor. There is no consensus on the optimal frequency of assessment, but an acceptable strategy would include periodic ultrasonographic monitoring of fetal growth and periodic fetal heart rate monitoring. A temperature elevation may indicate intrauterine infection. Prompt diagnosis of chorioamnionitis in preterm pregnancy requires a high index of suspicion because early signs and symptoms may be subtle. In the absence of fever, other clinical criteria have variable sensitivity and specificity for diagnosing infection. Serial monitoring of leukocyte counts and other markers of inflammation have not been proved to be useful and are nonspecific when there is no clinical evidence of infection, especially if antenatal corticosteroids have been administered (58). Specific management considerations regarding tocolytics, corticosteroids, antibiotics, magnesium sulfate, and timing of delivery are discussed in detail as follows.

▶ *Should tocolytics be considered for patients with preterm PROM?*

The use of tocolysis in the setting of preterm PROM is controversial and practice patterns among specialists vary widely (59). There are insufficient data to support or refute the use of prophylactic tocolysis in the setting of preterm PROM. A meta-analysis of eight trials that included 408 women is of limited use because women were only treated in two of the trials (60, 61) with latency antibiotics and corticosteroids, both of which have become part of standard management (62). The use of tocolysis was associated with a longer latency period and a lower risk of delivery within 48 hours but also was associated with a high risk of chorioamnionitis in pregnancies before 34 0/7 weeks of gestation. In summary, prophylactic tocolysis may be associated with a prolongation of pregnancy and an increased risk of chorioamnionitis without significant maternal or neonatal benefit, although its use has not been evaluated adequately with latency antibiotics and corticosteroids. In the setting of ruptured membranes with active labor, therapeutic tocolysis has not been shown to prolong latency or improve neonatal outcomes. Therefore, therapeutic tocolysis is not recommended (63).

▶ *Should antenatal corticosteroids be administered to patients with preterm PROM?*

The use of antenatal corticosteroids after preterm PROM has been evaluated in a number of clinical trials and has been shown to reduce neonatal mortality, respiratory distress syndrome, intraventricular hemorrhage, and necrotizing enterocolitis (64–66). Current data suggest that antenatal corticosteroids are not associated with increased risks of maternal or neonatal infection regardless of gestational age. A single course of corticosteroids is recommended for pregnant women between 24 0/7 weeks and 34 0/7 weeks of gestation, and may be considered for pregnant women as early as 23 0/7 weeks of gestation who are at risk of preterm delivery within 7 days (67, 68). A Cochrane meta-analysis reinforces the beneficial effect of this therapy regardless of membrane status and concludes that a single course of antenatal corticosteroids should be considered routine for all preterm deliveries (64).

Recent data indicate that administration of betamethasone in the late preterm period between 34 0/7 weeks and 36 6/7 weeks reduces respiratory morbidity in newborns (69). Although subgroup analysis was not done, approximately 20% of study patients had preterm PROM. It is assumed that patients with preterm PROM will benefit from betamethasone in the late preterm period, but because the study design excluded patients who had received corticosteroids earlier in the pregnancy, it is unknown whether there is any benefit to a second course of betamethasone in the late preterm period in these patients.

There are no data that support the use of corticosteroids before viability, and administration of corticosteroids in this setting is not currently recommended. Weekly administration of corticosteroids has been associated with a reduction in birth weight and head circumference and is not recommended (70–72). Whether to administer a rescue course of corticosteroids with PROM at any gestational age is controversial, and there is insufficient evidence to make a recommendation for or against.

▶ *Should magnesium sulfate for fetal neuroprotection be administered to patients with preterm PROM?*

Randomized controlled trials have demonstrated that maternal administration of magnesium sulfate used for fetal neuroprotection when birth is anticipated before 32 0/7 weeks of gestation reduces the risk of cerebral

palsy in surviving infants (RR, 0.71; 95% CI, 0.55–0.91) (73). In the largest of these trials, 85% of the women enrolled had preterm PROM between 24 weeks and 32 weeks of gestation (74). The optimal treatment regimen for fetal neuroprotection remains unclear, and different regimens were used in different trials. Hospitals that elect to use magnesium sulfate for fetal neuroprotection should develop uniform and specific guidelines for their departments regarding inclusion criteria, treatment regimens, concurrent tocolysis, and monitoring in accordance with one of the larger trials (74–76). Regardless of the treatment regimen used, women with preterm PROM before 32 0/7 weeks of gestation who are thought to be at risk of imminent delivery should be considered candidates for fetal neuroprotective treatment with magnesium sulfate.

▶ *Should antibiotics be administered to patients with preterm PROM?*

Administration of broad-spectrum antibiotics prolongs pregnancy, reduces maternal and neonatal infections, and reduces gestational age-dependent morbidity (16, 77, 78). The optimal antibiotic regimen is unclear because multiple regimens have demonstrated benefit. Based on available information, in order to reduce maternal and neonatal infections and gestational-age dependent morbidity, a 7-day course of therapy with a combination of intravenous ampicillin and erythromycin followed by oral amoxicillin and erythromycin is recommended during expectant management of women with preterm PROM who are less than 34 0/7 weeks of gestation (16, 77). The regimen used in the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development Maternal–Fetal Medicine Units Network trial was intravenous ampicillin (2 g every 6 hours) and erythromycin (250 mg every 6 hours) for 48 hours followed by oral amoxicillin (250 mg every 8 hours) and erythromycin base (333 mg every 8 hours) (78). The use of amoxicillin–clavulanic acid has been associated with increased rates of necrotizing enterocolitis and it is not recommended (16, 77). Although there are no well-studied alternative regimens for women allergic to β-lactam antibiotics, it may be reasonable to administer erythromycin alone. Women with preterm PROM and a viable fetus who are candidates for intrapartum GBS prophylaxis should receive intrapartum GBS prophylaxis to prevent vertical transmission regardless of earlier treatments (41, 79, 80).

▶ *Should preterm PROM be managed with home care?*

The outpatient management of preterm PROM with a viable fetus has not been sufficiently studied to establish safety and, therefore, is not recommended. Two small randomized controlled trials that compared hospitalization to home care of women with preterm PROM had insufficient power to demonstrate a meaningful difference in outcome because only 11–18% of the women were eligible for antepartum home care (81, 82). Because latency is frequently brief, infection may present suddenly and the fetus is at increased risk of umbilical cord compression, hospitalization with surveillance of the woman and her fetus is recommended once viability has been reached.

▶ *How should a patient with preterm PROM and a cervical cerclage be treated?*

There are no prospective studies with which to guide the care of women with preterm PROM who have a cervical cerclage. Results from retrospective studies have not been consistent, but generally have found that cerclage retention for more than 24 hours after preterm PROM is associated with pregnancy prolongation (83); however, because of the nonrandomized nature of the reports, it is unclear how factors such as labor or infection contributed to decisions for cerclage removal, which may have yielded biased results. In some, but not all studies, cerclage retention with preterm PROM has been associated with increased rates of neonatal mortality from sepsis, neonatal sepsis, respiratory distress syndrome, and maternal chorioamnionitis (83, 84).

A firm recommendation whether a cerclage should be removed after premature PROM cannot be made, and either removal or retention is reasonable. Regardless, if a cerclage remains in place with preterm PROM, prolonged antibiotic prophylaxis beyond 7 days is not recommended.

▶ *What is the optimal management of a patient with preterm PROM and herpes simplex virus infection or human immunodeficiency virus?*

Neonatal herpes simplex virus (HSV) infection usually results from maternal–fetal transmission during delivery. The risk of vertical transmission with delivery in primary HSV is reported to be between 30% and 50%, compared with only 3% in cases of recurrent HSV (85). The literature regarding expectant management of preterm PROM with active maternal HSV infection is limited to small case series and case reports (86, 87). All patients were treated with acyclovir, and cesarean delivery was performed if lesions were present at the time of delivery. No cases of vertical transmission were reported.

The risk of prematurity should be weighed against the potential risk of neonatal HSV infection. In the setting of PROM with recurrent active infection, expectant

management is recommended before 34 0/7 weeks of gestation. Herpes simplex virus therapy should be initiated, and corticosteroids, antibiotics, and magnesium sulfate for neuroprotection should be provided as clinically indicated. If active disease or prodromal symptoms are present at the onset of labor or when delivery is indicated, cesarean delivery is recommended.

Optimal management of preterm PROM in the setting of primary HSV infection is less clear because of the increased risk of vertical transmission. Herpes simplex virus therapy is recommended, and if lesions are present at the time of delivery, cesarean delivery is recommended.

The optimal management of the patient with human immunodeficiency virus (HIV) and preterm PROM is also uncertain because there are no adequate data from patients with prolonged rupture of the membranes. Early observations showed that the duration of membrane rupture in labor correlated with risk of transmission to the newborn (88), but current data suggest that the duration of membrane rupture is not correlated with risk of vertical transmission in patients who receive highly active antiretroviral therapy, have a low viral load, and receive antepartum and intrapartum zidovudine (89). Also, a series of 10 patients with preterm PROM who were managed expectantly while receiving antiretroviral therapy, had no cases of HIV transmission to the newborn despite viral loads as high as 23,000 copies per mL; the latent periods ranged from 4 hours to 4 days in this series, and all patients were delivered by cesarean (90).

The management of patients with HIV infection who have preterm PROM should be individualized, with consideration of factors, including gestational age, current antiretroviral regimen, and viral load. In cases where the gestational age is very early, the patient is being treated with antiretroviral medications, and the viral load is low, a period of expectant management may be appropriate. In all cases, the patient should be managed in consultation with a physician with expertise in management of HIV in pregnancy. Furthermore, standard antepartum and intrapartum treatment guidelines should be followed and management choices should be fully discussed with the patient (91).

▶ *How does care differ for patients with PROM that occurs before neonatal viability?*

Women presenting with PROM before neonatal viability should be counseled regarding the risks and benefits of expectant management versus immediate delivery. Counseling should include a realistic appraisal of neonatal outcomes. Immediate delivery should be offered. Attempts should be made to provide parents with the most current and accurate information possible (92).

If the patient opts for expectant management and is clinically stable with no evidence of infection, outpatient surveillance can be considered. Precautions should be reviewed with the patient and she should come to the hospital if she develops symptoms of infection, labor, or abruptio placentae. It may be useful to instruct patients to monitor temperatures. Typically, women with previable PROM who have been cared for as outpatients are admitted to the hospital once the pregnancy has reached viability.

Administration of antenatal corticosteroids and latency antibiotics for fetal maturation upon reaching viability is appropriate given that early delivery remains likely. Multiple ultrasonographic methods (such as thoracic measurements and ratios, flow velocities in pulmonary vessels, and three-dimensional estimations of lung volume) have been studied to evaluate pulmonary development in the antepartum period, but all are of limited accuracy and cannot be considered sufficiently reliable for clinical management (30). Because most studies of antibiotic prophylaxis with preterm PROM enrolled patients only after 24 0/7 weeks of gestation, there are no adequate data to assess the risks and benefits of such treatment at earlier gestational ages. However, it is reasonable to offer a course of antibiotics for the pregnancy prolongation to patients with previable PROM who choose expectant management (67). There is no evidence to support the use of tocolytics in the setting of previable preterm PROM, and in this setting, tocolysis is not recommended.

▶ *What is the expected outcome of PROM after second-trimester amniocentesis?*

In studies of women undergoing second-trimester amniocentesis for prenatal diagnosis of genetic disorders, the risk of PROM is approximately 1% (93, 94). In contrast to patients with spontaneous PROM in the second trimester, reaccumulation of normal amniotic fluid volume and favorable outcomes are expected. In one series of 11 patients with PROM after genetic amniocentesis, there was one previable pregnancy loss, reaccumulation of normal amniotic fluid occurred within 1 month in 72% of patients, and the perinatal survival rate was 91% (93).

After appropriate counseling, patients with PROM after genetic amniocentesis typically are managed expectantly as outpatients. Precautions regarding symptoms of chorioamnionitis and miscarriage should be given. Regular follow-up visits with ultrasonographic examinations to assess amniotic fluid volume are recommended.

- ***How should a patient with a history of preterm PROM be managed in future pregnancies?***

Patients with prior preterm PROM have an increased risk of recurrent PROM and preterm birth, and a detailed medical history should be taken. However, there are few studies that examine interventions to prevent recurrent PROM. Patients with a history of preterm PROM were included in studies of progesterone supplementation for preterm birth recurrence reduction, but most studies did not report the specific proportion of women with PROM in the study group or separately analyze results in those patients (95, 96). However, given the potential benefit of progesterone therapy, women with a single gestation and a prior spontaneous preterm birth (due to either labor with intact membranes or PROM) should be offered progesterone supplementation starting at 16 weeks to 24 weeks of gestation to reduce the risk of recurrent spontaneous preterm birth.

Although vaginal ultrasonographic measurement of the cervix is a safe and reliable means of evaluating the risk of preterm birth related to cervical length, there have been no well-designed trials of cervical surveillance in women with a history of PROM. Similar to the progesterone studies, women with prior PROM were included in trials that evaluated cervical assessment, vaginal progesterone, and cerclage but their specific data were not reported (97, 98). Thus, as with women with spontaneous preterm births, consideration can be given to transvaginal cervical length screening. Cerclage placement is associated with significant decreases in preterm birth outcomes, offers perinatal benefits, and may be considered in women with the following combination of history and ultrasound findings: a current singleton pregnancy, prior spontaneous preterm birth at less than 34 weeks of gestation, and short cervical length (less than 25 mm) before 24 weeks of gestation (99). There are no data on which to base a recommendation regarding the optimal gestational age for initiating surveillance or frequency of monitoring.

Summary of Recommendations and Conclusions

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

- Patients with PROM before 34 0/7 weeks of gestation should be managed expectantly if no maternal or fetal contraindications exist.
- To reduce maternal and neonatal infections and gestational-age dependent morbidity, a 7-day course of therapy with a combination of intravenous ampicillin and erythromycin followed by oral amoxicillin and erythromycin is recommended during expectant management of women with preterm PROM who are less than 34 0/7 weeks of gestation.
- Women with preterm PROM and a viable fetus who are candidates for intrapartum GBS prophylaxis should receive intrapartum GBS prophylaxis to prevent vertical transmission regardless of earlier treatments.
- A single course of corticosteroids is recommended for pregnant women between 24 0/7 weeks and 34 0/7 weeks of gestation, and may be considered for pregnant women as early as 23 0/7 weeks of gestation who are at risk of preterm delivery within 7 days.
- Women with preterm PROM before 32 0/7 weeks of gestation who are thought to be at risk of imminent delivery should be considered candidates for fetal neuroprotective treatment with magnesium sulfate.

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

- For women with PROM at 37 0/7 weeks of gestation or more, if spontaneous labor does not occur near the time of presentation in those who do not have contraindications to labor, labor should be induced.
- At 34 0/7 weeks or greater gestation, delivery is recommended for all women with ruptured membranes.
- In the setting of ruptured membranes with active labor, therapeutic tocolysis has not been shown to prolong latency or improve neonatal outcomes. Therefore, therapeutic tocolysis is not recommended.

The following conclusion is based primarily on consensus and expert opinion (Level C):

- The outpatient management of preterm PROM with a viable fetus has not been sufficiently studied to establish safety and, therefore, is not recommended.

Proposed Performance Measure

The percentage of expectantly managed patients with preterm PROM (up to 34 0/7 weeks of gestation) that receive latency antibiotics and corticosteroids

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The MEDLINE database, the Cochrane Library, and the American College of Obstetricians and Gynecologists' own internal resources and documents were used to conduct a literature search to locate relevant articles published between January 1990–June 2013. The search was restricted to articles published in the English language. Priority was given to articles reporting results of original research, although review articles and commentaries also were consulted. Abstracts of research presented at symposia and scientific conferences were not considered adequate for inclusion in this document. Guidelines published by organizations or institutions such as the National Institutes of Health and the American College of Obstetricians and Gynecologists were reviewed, and additional studies were located by reviewing bibliographies of identified articles. When reliable research was not available, expert opinions from obstetrician–gynecologists were used.

Studies were reviewed and evaluated for quality according to the method outlined by the U.S. Preventive Services Task Force:

I	Evidence obtained from at least one properly designed randomized controlled trial.
II-1	Evidence obtained from well-designed controlled trials without randomization.
II-2	Evidence obtained from well-designed cohort or case–control analytic studies, preferably from more than one center or research group.
II-3	Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments also could be regarded as this type of evidence.
III	Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

Based on the highest level of evidence found in the data, recommendations are provided and graded according to the following categories:

Level A—Recommendations are based on good and consistent scientific evidence.

Level B—Recommendations are based on limited or inconsistent scientific evidence.

Level C—Recommendations are based primarily on consensus and expert opinion.

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