



PRACTICE BULLETIN

CLINICAL MANAGEMENT GUIDELINES FOR OBSTETRICIAN—GYNECOLOGISTS

NUMBER 160, JANUARY 2016

(Replaces Practice Bulletin Number 139, October 2013)

INTERIM UPDATE: This Practice Bulletin is updated to reflect a limited, focused change in gestational age at which to consider antenatal corticosteroids.

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

Committee on Practice Bulletins—Obstetrics. This Practice Bulletin was developed by the Committee on Practice Bulletins—Obstetrics with the assistance of Robert Ehsanipoor, MD. The information is designed to aid practitioners in making decisions about appropriate obstetric and gynecologic care. These guidelines should not be construed as dictating an exclusive course of treatment or procedure. Variations in practice may be warranted based on the needs of the individual patient, resources, and limitations unique to the institution or type of practice.



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).

Previale 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 benefited 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

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.

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 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 corticosteroid administration 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 (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). 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 (69–71). Whether to administer a rescue course of corticosteroids with PROM 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) (72). In the largest of these trials, 85% of the women enrolled had preterm PROM between 24 weeks and 32 weeks of gestation (73). 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 (73–75). 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, 76, 77). 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, 76). 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) (77). The use of amoxicillin–clavulanic acid has been associated with increased rates of necrotizing enterocolitis and it is not recommended (16, 76). 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, 78, 79).

► ***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 (80, 81). 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 (82); 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 (82, 83).

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 (84). The literature regarding expectant management of preterm PROM with active maternal HSV infection is limited to small case series and case reports (85, 86). 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 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 (87), 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 (88). 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 (89).

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 (90).

► ***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 (91).

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% (92, 93). 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% (92).

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 (94, 95). 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 (96, 97). 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 (98). 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 erythromycin and ampicillin or amoxicillin 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.
- ▶ 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 intravenous 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

References

1. Martin JA, Hamilton BE, Ventura SJ, Osterman MJ, Wilson EC, Mathews TJ. Births: final data for 2010. Natl Vital Stat Rep 2012;61(1):1–71. (Level II-3) ⇐
2. Mathews TJ, MacDorman MF. Infant mortality statistics from the 2006 period linked birth/infant death data set. Natl Vital Stat Rep 2010;58:1–31. (Level II-3) [PubMed] ⇐
3. Waters TP, Mercer B. Preterm PROM: prediction, prevention, principles. Clin Obstet Gynecol 2011;54:307–12. (Level III) [PubMed] ⇐



4. Moore RM, Mansour JM, Redline RW, Mercer BM, Moore JJ. The physiology of fetal membrane rupture: insight gained from the determination of physical properties. *Placenta* 2006;27:1037–51. (Level III) [PubMed] ⇐
5. Mercer BM. Preterm premature rupture of the membranes. *Obstet Gynecol* 2003;101:178–93. (Level III) [PubMed] [*Obstetrics & Gynecology*] ⇐
6. Garite TJ, Freeman RK. Chorioamnionitis in the preterm gestation. *Obstet Gynecol* 1982;59:539–45. (Level II-3) [PubMed] [*Obstetrics & Gynecology*] ⇐
7. Mercer BM, Goldenberg RL, Moawad AH, Meis PJ, Iams JD, Das AF, et al. The preterm prediction study: effect of gestational age and cause of preterm birth on subsequent obstetric outcome. National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network. *Am J Obstet Gynecol* 1999;181:1216–21. (Level II-2) [PubMed] ⇐
8. Asrat T, Lewis DF, Garite TJ, Major CA, Nageotte MP, Towers CV, et al. Rate of recurrence of preterm premature rupture of membranes in consecutive pregnancies. *Am J Obstet Gynecol* 1991;165:1111–5. (Level II-2) [PubMed] ⇐
9. Mercer BM, Goldenberg RL, Meis PJ, Moawad AH, Shellhaas C, Das A, et al. The Preterm Prediction Study: prediction of preterm premature rupture of membranes through clinical findings and ancillary testing. The National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network. *Am J Obstet Gynecol* 2000;183:738–45. (Level II-2) [PubMed] [Full Text] ⇐
10. Harger JH, Hsing AW, Tuomala RE, Gibbs RS, Mead PB, Eschenbach DA, et al. Risk factors for preterm premature rupture of fetal membranes: a multicenter case-control study. *Am J Obstet Gynecol* 1990;163:130–7. (Level II-2) [PubMed] ⇐
11. Berkowitz GS, Blackmore-Prince C, Lapinski RH, Savitz DA. Risk factors for preterm birth subtypes. *Epidemiology* 1998;9:279–85. (Level II-3) [PubMed] ⇐
12. Treadwell MC, Bronsteen RA, Bottoms SF. Prognostic factors and complication rates for cervical cerclage: a review of 482 cases. *Am J Obstet Gynecol* 1991;165:555–8. (Level II-3) [PubMed] ⇐
13. Hannah ME, Ohlsson A, Farine D, Hewson SA, Hodnett ED, Myhr TL, et al. Induction of labor compared with expectant management for prelabor rupture of the membranes at term. TERMPROM Study Group. *N Engl J Med* 1996;334:1005–10. (Level I) [PubMed] [Full Text] ⇐
14. Melamed N, Hadar E, Ben-Haroush A, Kaplan B, Yogev Y. Factors affecting the duration of the latency period in preterm premature rupture of membranes. *J Matern Fetal Neonatal Med* 2009;22:1051–6. (Level II-3) [PubMed] [Full Text] ⇐
15. Johnson JW, Egerman RS, Moorhead J. Cases with ruptured membranes that “re-seal”. *Am J Obstet Gynecol* 1990;163:1024–30; discussion 1030–2. (Level II-2) [PubMed] ⇐
16. Kenyon S, Boulvain M, Neilson JP. Antibiotics for preterm rupture of membranes. *Cochrane Database of Systematic Reviews* 2010, Issue 8. Art. No.: CD001058. DOI: 10.1002/14651858.CD001058.pub2. (Meta-analysis) [PubMed] [Full Text] ⇐
17. Beydoun SN, Yasin SY. Premature rupture of the membranes before 28 weeks: conservative management. *Am J Obstet Gynecol* 1986;155:471–9. (Level III) [PubMed] ⇐
18. Major CA, de Veciana M, Lewis DF, Morgan MA. Preterm premature rupture of membranes and abruptio placentae: is there an association between these pregnancy complications? *Am J Obstet Gynecol* 1995;172:672–6. (Level II-3) [PubMed] [Full Text] ⇐
19. Ananth CV, Oyelese Y, Srinivas N, Yeo L, Vintzileos AM. Preterm premature rupture of membranes, intra-uterine infection, and oligohydramnios: risk factors for placental abruption. *Obstet Gynecol* 2004;104:71–7. (Level II-3) [PubMed] [*Obstetrics & Gynecology*] ⇐
20. Lemons JA, Bauer CR, Oh W, Korones SB, Papile LA, Stoll BJ, et al. Very low birth weight outcomes of the National Institute of Child health and human development neonatal research network, January 1995 through December 1996. NICHD Neonatal Research Network. *Pediatrics* 2001;107:E1. (Level II-3) [PubMed] [Full Text] ⇐
21. Spinillo A, Capuzzo E, Stronati M, Ometto A, Orcesi S, Fazzi E. Effect of preterm premature rupture of membranes on neurodevelopmental outcome: follow up at two years of age. *Br J Obstet Gynaecol* 1995;102:882–7. (Level II-2) [PubMed] ⇐
22. Yoon BH, Romero R, Park JS, Kim CJ, Kim SH, Choi JH, et al. Fetal exposure to an intra-amniotic inflammation and the development of cerebral palsy at the age of three years. *Am J Obstet Gynecol* 2000;182:675–81. (Level II-2) [PubMed] ⇐
23. Locatelli A, Ghidini A, Paterlini G, Patane L, Doria V, Zorloni C, et al. Gestational age at preterm premature rupture of membranes: a risk factor for neonatal white matter damage. *Am J Obstet Gynecol* 2005;193:947–51. (Level II-3) [PubMed] [Full Text] ⇐
24. Mercer BM, Arheart KL. Antimicrobial therapy in expectant management of preterm premature rupture of the membranes [published erratum appears in *Lancet* 1996;347:410]. *Lancet* 1995;346:1271–9. (Meta-analysis) [PubMed] [Full Text] ⇐
25. Manuck TA, Eller AG, Esplin MS, Stoddard GJ, Varner MW, Silver RM. Outcomes of expectantly managed preterm premature rupture of membranes occurring before 24 weeks of gestation. *Obstet Gynecol* 2009;114:29–37. (Level II-3) [PubMed] [*Obstetrics & Gynecology*] ⇐
26. Waters TP, Mercer BM. The management of preterm premature rupture of the membranes near the limit of fetal viability. *Am J Obstet Gynecol* 2009;201:230–40. (Level III) [PubMed] [Full Text] ⇐
27. Schucker JL, Mercer BM. Midtrimester premature rupture of the membranes. *Semin Perinatol* 1996;20:389–400. (Level III) [PubMed] ⇐
28. Muris C, Girard B, Creveuil C, Durin L, Herlicoviez M, Dreyfus M. Management of premature rupture of membranes before 25 weeks. *Eur J Obstet Gynecol Reprod Biol* 2007;131:163–8. (Level III) [PubMed] [Full Text] ⇐



29. Farooqi A, Holmgren PA, Engberg S, Serenius F. Survival and 2-year outcome with expectant management of second-trimester rupture of membranes. *Obstet Gynecol* 1998;92:895–901. (Level II-3) [PubMed] [*Obstetrics & Gynecology*] ↵
30. van Teeffelen AS, van der Ham DP, Oei SG, Porath MM, Willekes C, Mol BW. The accuracy of clinical parameters in the prediction of perinatal pulmonary hypoplasia secondary to midtrimester prelabour rupture of fetal membranes: a meta-analysis. *Eur J Obstet Gynecol Reprod Biol* 2010;148:3–12. (Meta-analysis) [PubMed] [Full Text] ↵
31. van Teeffelen AS, Van Der Heijden J, Oei SG, Porath MM, Willekes C, Opmeer B, et al. Accuracy of imaging parameters in the prediction of lethal pulmonary hypoplasia secondary to mid-trimester prelabor rupture of fetal membranes: a systematic review and meta-analysis. *Ultrasound Obstet Gynecol* 2012;39:495–9. (Meta-analysis) [PubMed] [Full Text] ↵
32. Blott M, Greenough A. Neonatal outcome after prolonged rupture of the membranes starting in the second trimester. *Arch Dis Child* 1988;63:1146–50. (Level III) [PubMed] [Full Text] ↵
33. Alexander JM, Mercer BM, Miodovnik M, Thurnau GR, Goldenberg RL, Das AF, et al. The impact of digital cervical examination on expectantly managed preterm rupture of membranes. *Am J Obstet Gynecol* 2000;183:1003–7. (Level II-2) [PubMed] [Full Text] ↵
34. Munson LA, Graham A, Koos BJ, Valenzuela GJ. Is there a need for digital examination in patients with spontaneous rupture of the membranes? *Am J Obstet Gynecol* 1985;153:562–3. (Level III) [PubMed] ↵
35. Eriksen NL, Parisi VM, Daoust S, Flamm B, Garite TJ, Cox SM. Fetal fibronectin: a method for detecting the presence of amniotic fluid. *Obstet Gynecol* 1992;80:451–4. (Level II-2) [PubMed] [*Obstetrics & Gynecology*] ↵
36. Lee SE, Park JS, Norwitz ER, Kim KW, Park HS, Jun JK. Measurement of placental alpha-microglobulin-1 in cervicovaginal discharge to diagnose rupture of membranes. *Obstet Gynecol* 2007;109:634–40. (Level II-3) [PubMed] [*Obstetrics & Gynecology*] ↵
37. Cousins LM, Smok DP, Lovett SM, Poeltler DM. AmniSure placental alpha microglobulin-1 rapid immunoassay versus standard diagnostic methods for detection of rupture of membranes. *Am J Perinatol* 2005;22:317–20. (Level II-3) [PubMed] [Full Text] ↵
38. Lee SM, Lee J, Seong HS, Lee SE, Park JS, Romero R, et al. The clinical significance of a positive Amnisure test in women with term labor with intact membranes. *J Matern Fetal Neonatal Med* 2009;22:305–10. (Level II-3) [PubMed] [Full Text] ↵
39. Lee SM, Romero R, Park JW, Kim SM, Park CW, Korzeniewski SJ, et al. The clinical significance of a positive Amnisure test in women with preterm labor and intact membranes. *J Matern Fetal Neonatal Med* 2012;25:1690–8. (Level II-2) [PubMed] [Full Text] ↵
40. Smith CV, Greenspoon J, Phelan JP, Platt LD. Clinical utility of the nonstress test in the conservative management of women with preterm spontaneous premature rupture of the membranes. *J Reprod Med* 1987;32:1–4. (Level II-3) [PubMed] ↵
41. Verani JR, McGee L, Schrag SJ. Prevention of perinatal group B streptococcal disease—revised guidelines from CDC, 2010. Division of Bacterial Diseases, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention (CDC). *MMWR Recomm Rep* 2010;59(RR-10):1–36. (Level I) [PubMed] [Full Text] ↵
42. Dare MR, Middleton P, Crowther CA, Flenady V, Varatharaju B. Planned early birth versus expectant management (waiting) for prelabour rupture of membranes at term (37 weeks or more). *Cochrane Database of Systematic Reviews* 2006, Issue 1. Art. No.: CD005302. DOI: 10.1002/14651858.CD005302.pub2. (Meta-analysis) [PubMed] [Full Text] ↵
43. Flenady V, King JF. Antibiotics for prelabour rupture of membranes at or near term. *Cochrane Database of Systematic Reviews* 2002, Issue 3. Art. No.: CD001807. DOI: 10.1002/14651858.CD001807. (Meta-analysis) [PubMed] [Full Text] ↵
44. Ovalle A, Martinez MA, Kakarieka E, Gomez R, Rubio R, Valderrama O, et al. Antibiotic administration in patients with preterm premature rupture of membranes reduces the rate of histological chorioamnionitis: a prospective, randomized, controlled study. *J Matern Fetal Neonatal Med* 2002;12:35–41. (Level I) [PubMed] [Full Text] ↵
45. Cararach V, Botet F, Sentis J, Almirall R, Perez-Picanol E. Administration of antibiotics to patients with rupture of membranes at term: a prospective, randomized, multicentric study. Collaborative Group on PROM. *Acta Obstet Gynecol Scand* 1998;77:298–302. (Level I) [PubMed] [Full Text] ↵
46. Rouse DJ, Weiner SJ, Bloom SL, Varner MW, Spong CY, Ramin SM, et al. Failed labor induction: toward an objective diagnosis. Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) Maternal-Fetal Medicine Units Network (MFMU). *Obstet Gynecol* 2011;117:267–72. (Level III) [PubMed] [*Obstetrics & Gynecology*] ↵
47. Rouse DJ, Owen J, Hauth JC. Criteria for failed labor induction: prospective evaluation of a standardized protocol. *Obstet Gynecol* 2000;96:671–7. (Level II-3) [PubMed] [*Obstetrics & Gynecology*] ↵
48. Simon CE, Grobman WA. When Has an Induction Failed? *Obstet Gynecol* 2005;105:705–9. (Level II-2) [PubMed] [*Obstetrics & Gynecology*] ↵
49. Buchanan SL, Crowther CA, Levett KM, Middleton P, Morris J. Planned early birth versus expectant management for women with preterm prelabour rupture of membranes prior to 37 weeks' gestation for improving pregnancy outcome. *Cochrane Database of Systematic Reviews* 2010, Issue 3. Art. No.: CD004735. DOI: 10.1002/14651858.CD004735.pub3. (Meta-analysis) [PubMed] [Full Text] ↵
50. van der Ham DP, van der Heyden JL, Opmeer BC, Mulder AL, Moonen RM, van Beek JH, et al. Management of late-preterm premature rupture of membranes: the



- PPROMEXIL-2 trial. *Am J Obstet Gynecol* 2012;207:276.e1–276.10. (Level I) [PubMed] [Full Text] ↵
51. van der Ham DP, Vijgen SM, Nijhuis JG, van Beek JJ, Opmeer BC, Mulder AL, et al. Induction of labor versus expectant management in women with preterm prelabor rupture of membranes between 34 and 37 weeks: a randomized controlled trial. PROMEXIL trial group. *PLoS Med* 2012;9:e1001208. (Level I) [PubMed] [Full Text] ↵
 52. Naef RW 3rd, Allbert JR, Ross EL, Weber BM, Martin RW, Morrison JC. Premature rupture of membranes at 34 to 37 weeks' gestation: aggressive versus conservative management. *Am J Obstet Gynecol* 1998;178:126–30. (Level I) [PubMed] ↵
 53. Mercer BM, Crocker LG, Boe NM, Sibai BM. Induction versus expectant management in premature rupture of the membranes with mature amniotic fluid at 32 to 36 weeks: a randomized trial. *Am J Obstet Gynecol* 1993;169:775–82. (Level I) [PubMed] ↵
 54. Teune MJ, Bakhuizen S, Gyamfi Bannerman C, Opmeer BC, van Kaam AH, van Wassenaer AG, et al. A systematic review of severe morbidity in infants born late preterm. *Am J Obstet Gynecol* 2011;205:374.e1–374.e9. (Meta-analysis) [PubMed] [Full Text] ↵
 55. McGowan JE, Alderdice FA, Holmes VA, Johnston L. Early childhood development of late-preterm infants: a systematic review. *Pediatrics* 2011;127:1111–24. (Level III) [PubMed] [Full Text] ↵
 56. Melamed N, Ben-Haroush A, Pardo J, Chen R, Hadar E, Hod M, et al. Expectant management of preterm premature rupture of membranes: is it all about gestational age? *Am J Obstet Gynecol* 2011;204:48.e1–48.e8. (Level II-3) [PubMed] [Full Text] ↵
 57. Ramsey PS, Lieman JM, Brumfield CG, Carlo W. Chorioamnionitis increases neonatal morbidity in pregnancies complicated by preterm premature rupture of membranes. *Am J Obstet Gynecol* 2005;192:1162–6. (Level II-3) [PubMed] [Full Text] ↵
 58. Tita AT, Andrews WW. Diagnosis and management of clinical chorioamnionitis. *Clin Perinatol* 2010;37:339–54. (Level III) [PubMed] [Full Text] ↵
 59. Fox NS, Gelber SE, Kalish RB, Chasen ST. Contemporary practice patterns and beliefs regarding tocolysis among U.S. maternal-fetal medicine specialists. *Obstet Gynecol* 2008;112:42–7. (Level III) [PubMed] [*Obstetrics & Gynecology*] ↵
 60. Dunlop PD, Crowley PA, Lamont RF, Hawkins DF. Preterm ruptured membranes, no contractions. *J Obstet Gynaecol* 1986;7:92–6. (Level II-1) ↵
 61. Ehsanipoor RM, Shrivastava VK, Lee RM, Chan K, Galyean AM, Garite TJ, et al. A randomized, double-masked trial of prophylactic indomethacin tocolysis versus placebo in women with premature rupture of membranes. *Am J Perinatol* 2011;28:473–8. (Level I) [PubMed] [Full Text] ↵
 62. Mackeen AD, Seibel-Seamon J, Grimes-Dennis J, Baxter JK, Berghella V. Tocolytics for preterm premature rupture of membranes. *Cochrane Database of Systematic Reviews* 2011, Issue 10. Art. No.: CD007062. DOI: 10.1002/14651858.CD007062.pub2. (Meta-analysis) [PubMed] [Full Text] ↵
 63. Garite TJ, Keegan KA, Freeman RK, Nageotte MP. A randomized trial of ritodrine tocolysis versus expectant management in patients with premature rupture of membranes at 25 to 30 weeks of gestation. *Am J Obstet Gynecol* 1987;157:388–93. (Level I) [PubMed] ↵
 64. Roberts D, Dalziel SR. Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth. *Cochrane Database of Systematic Reviews* 2006, Issue 3. Art. No.: CD004454. DOI: 10.1002/14651858.CD004454.pub2. (Meta-analysis) [PubMed] [Full Text] ↵
 65. Vidaeff AC, Ramin SM. Antenatal corticosteroids after preterm premature rupture of membranes. *Clin Obstet Gynecol* 2011;54:337–43. (Level III) [PubMed] ↵
 66. Harding JE, Pang J, Knight DB, Liggins GC. Do antenatal corticosteroids help in the setting of preterm rupture of membranes? *Am J Obstet Gynecol* 2001; 184:131–9. (Level II-2) [PubMed] [Full Text] ↵
 67. Periviable Birth. *Obstetric Care Consensus No. 3. American College of Obstetricians and Gynecologists. Obstet Gynecol* 2015;126:e82–94. (Level III) [PubMed] [*Obstetrics & Gynecology*] ↵
 68. Antenatal corticosteroids revisited: repeat courses. *NIH Consens Statement* 2000;17(2):1–18. (Level III) [PubMed] ↵
 69. Wapner RJ, Sorokin Y, Thom EA, Johnson F, Dudley DJ, Spong CY, et al. Single versus weekly courses of antenatal corticosteroids: evaluation of safety and efficacy. National Institute of Child Health and Human Development Maternal Fetal Medicine Units Network. *Am J Obstet Gynecol* 2006;195:633–42. (Level I) [PubMed] [Full Text] ↵
 70. Bloom SL, Sheffield JS, McIntire DD, Leveno KJ. Antenatal dexamethasone and decreased birth weight. *Obstet Gynecol* 2001;97:485–90. (Level II-3) [PubMed] [*Obstetrics & Gynecology*] ↵
 71. Thorp JA, Jones PG, Knox E, Clark RH. Does antenatal corticosteroid therapy affect birth weight and head circumference? *Obstet Gynecol* 2002;99:101–8. (Level II-3) [PubMed] [*Obstetrics & Gynecology*] ↵
 72. Doyle LW, Crowther CA, Middleton P, Marret S, Rouse D. Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus. *Cochrane Database of Systematic Reviews* 2009, Issue 1. Art. No.: CD004661. DOI: 10.1002/14651858.CD004661.pub3. (Meta-analysis) [PubMed] [Full Text] ↵
 73. Rouse DJ, Hirtz DG, Thom E, Varner MW, Spong CY, Mercer BM, et al. A randomized, controlled trial of magnesium sulfate for the prevention of cerebral palsy. Eunice Kennedy Shriver NICHD Maternal-Fetal Medicine Units Network. *N Engl J Med* 2008;359:895–905. (Level I) [PubMed] [Full Text] ↵
 74. Marret S, Marpeau L, Zupan-Simunek V, Eurin D, Leveque C, Hellot MF, et al. Magnesium sulphate given before very-preterm birth to protect infant brain: the randomised controlled PREMAG trial. PREMAG trial group. *BJOG* 2007;114:310–8. (Level I) [PubMed] [Full Text] ↵



75. Crowther CA, Hiller JE, Doyle LW, Haslam RR. Effect of magnesium sulfate given for neuroprotection before preterm birth: a randomized controlled trial. Australasian Collaborative Trial of Magnesium Sulphate (ACTOMg SO4) Collaborative Group. *JAMA* 2003;290:2669–76. (Level I) [PubMed] [Full Text] ↵
76. Kenyon SL, Taylor DJ, Tarnow-Mordi W. Broad-spectrum antibiotics for preterm, prelabour rupture of fetal membranes: the ORACLE I randomised trial. ORACLE Collaborative Group [published erratum appears in *Lancet* 2001;358:156]. *Lancet* 2001;357:979–88. (Level I) [PubMed] [Full Text] ↵
77. Mercer BM, Miodovnik M, Thurnau GR, Goldenberg RL, Das AF, Ramsey RD, et al. Antibiotic therapy for reduction of infant morbidity after preterm premature rupture of the membranes. A randomized controlled trial. National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network. *JAMA* 1997;278:989–95. (Level I) [PubMed] ↵
78. Prevention of early-onset group B streptococcal disease in newborns. Committee Opinion No. 485. American College of Obstetricians and Gynecologists. *Obstet Gynecol* 2011;117:1019–27. (Level III) [PubMed] [*Obstetrics & Gynecology*] ↵
79. Use of prophylactic antibiotics in labor and delivery. Practice Bulletin No. 120. American College of Obstetricians and Gynecologists. *Obstet Gynecol* 2011;117:1472–83. (Level III) [PubMed] [*Obstetrics & Gynecology*] ↵
80. Abou El Senoun G, Dowswell T, Mousa HA. Planned home versus hospital care for preterm prelabour rupture of the membranes (PPROM) prior to 37 weeks' gestation. *Cochrane Database of Systematic Reviews* 2010, Issue 4. Art. No.: CD008053. DOI: 10.1002/14651858.CD008053.pub2. (Meta-analysis) [PubMed] [Full Text] ↵
81. Carlan SJ, O'Brien WF, Parsons MT, Lense JJ. Preterm premature rupture of membranes: a randomized study of home versus hospital management. *Obstet Gynecol* 1993;81:61–4. (Level I) [PubMed] [*Obstetrics & Gynecology*] ↵
82. Giraldo-Isaza MA, Berghella V. Cervical cerclage and preterm PROM. *Clin Obstet Gynecol* 2011;54:313–20. (Level III) [PubMed] ↵
83. Laskin MD, Yinon Y, Whittle WL. Preterm premature rupture of membranes in the presence of cerclage: is the risk for intra-uterine infection and adverse neonatal outcome increased? *J Matern Fetal Neonatal Med* 2012;25:424–8. (Level II-2) [PubMed] [Full Text] ↵
84. Brown ZA, Gardella C, Wald A, Morrow RA, Corey L. Genital herpes complicating pregnancy [published errata appear in *Obstet Gynecol* 2006;107:428; *Obstet Gynecol* 2007;109:207]. *Obstet Gynecol* 2005;106:845–56. (Level III) [PubMed] [*Obstetrics & Gynecology*] ↵
85. Ehsanipoor RM, Major CA. Herpes simplex and HIV infections and preterm PROM. *Clin Obstet Gynecol* 2011;54:330–6. (Level III) [PubMed] ↵
86. Major CA, Towers CV, Lewis DF, Garite TJ. Expectant management of preterm premature rupture of membranes complicated by active recurrent genital herpes. *Am J Obstet Gynecol* 2003;188:1551–4; discussion 1554–5. (Level II-3) [PubMed] [Full Text] ↵
87. Landesman SH, Kalish LA, Burns DN, Minkoff H, Fox HE, Zorrilla C, et al. Obstetrical factors and the transmission of human immunodeficiency virus type 1 from mother to child. The Women and Infants Transmission Study. *N Engl J Med* 1996;334:1617–23. (Level II-2) [PubMed] [Full Text] ↵
88. Cotter AM, Brookfield KF, Duthely LM, Gonzalez Quintero VH, Potter JE, O'Sullivan MJ. Duration of membrane rupture and risk of perinatal transmission of HIV-1 in the era of combination antiretroviral therapy. *Am J Obstet Gynecol* 2012;207:482.e1–5. (Level II-2) [PubMed] [Full Text] ↵
89. Alvarez JR, Bardeguez A, Iffy L, Apuzzio JJ. Preterm premature rupture of membranes in pregnancies complicated by human immunodeficiency virus infection: a single center's five-year experience. *J Matern Fetal Neonatal Med* 2007;20:853–7. (Level II-3) [PubMed] [Full Text] ↵
90. Panel on Treatment of HIV-Infected Pregnant Women and Prevention of Perinatal Transmission. Recommendations for use of antiretroviral drugs in pregnant HIV-1-infected women for maternal health and interventions to reduce perinatal HIV transmission in the United States. Rockville (MD): Department of Health and Human Services. Available at <http://aidsinfo.nih.gov/contentfiles/lvguidelines/perinatalGL.pdf>. Retrieved July 30, 2013. (Level III) ↵
91. Perinatal care at the threshold of viability. ACOG Practice Bulletin No. 38. American College of Obstetricians and Gynecologists; *Obstet Gynecol* 2002;100:617–24. (Level III) [PubMed] [*Obstetrics & Gynecology*] ↵
92. Borgida AF, Mills AA, Feldman DM, Rodis JF, Egan JF. Outcome of pregnancies complicated by ruptured membranes after genetic amniocentesis. *Am J Obstet Gynecol* 2000;183:937–9. (Level II-3) [PubMed] [Full Text] ↵
93. Gold RB, Goyert GL, Schwartz DB, Evans MI, Seabolt LA. Conservative management of second-trimester post-amniocentesis fluid leakage. *Obstet Gynecol* 1989;74:745–7. (Level III) [PubMed] [*Obstetrics & Gynecology*] ↵
94. Meis PJ, Klebanoff M, Thom E, Dombrowski MP, Sibai B, Moawad AH, et al. Prevention of recurrent preterm delivery by 17 alpha-hydroxyprogesterone caproate. National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network [published erratum appears in *N Engl J Med* 2003;349:1299]. *N Engl J Med* 2003;348:2379–85. (Level I) [PubMed] [Full Text] ↵
95. Tita AT, Rouse DJ. Progesterone for preterm birth prevention: an evolving intervention. *Am J Obstet Gynecol* 2009;200:219–24. (Level III) [PubMed] [Full Text] ↵
96. Hassan SS, Romero R, Vidyadhari D, Fusey S, Baxter JK, Khandelwal M, et al. Vaginal progesterone reduces the rate of preterm birth in women with a sonographic short cervix: a multicenter, randomized, double-blind,



placebo-controlled trial. PREGNANT Trial. *Ultrasound Obstet Gynecol* 2011;38:18–31. (Level I) [PubMed] [Full Text] ⇐

97. Owen J, Hankins G, Iams JD, Berghella V, Sheffield JS, Perez-Delboy A, et al. Multicenter randomized trial of cerclage for preterm birth prevention in high-risk women with shortened midtrimester cervical length. *Am J Obstet Gynecol* 2009;201:375.e1–375.e8. (Level I) [PubMed] [Full Text] ⇐
98. Berghella V, Rafael TJ, Szychowski JM, Rust OA, Owen J. Cerclage for short cervix on ultrasonography in women with singleton gestations and previous preterm birth: a meta-analysis. *Obstet Gynecol* 2011;117:663–71. (Meta-analysis) [PubMed] [*Obstetrics & Gynecology*] ⇐

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.

Copyright January 2016 by the American College of Obstetricians and Gynecologists. All rights reserved. No part of this publication may be reproduced, stored in a retrieval system, posted on the Internet, or transmitted, in any form or by any means, electronic, mechanical, photocopying, recording, or otherwise, without prior written permission from the publisher.

Requests for authorization to make photocopies should be directed to Copyright Clearance Center, 222 Rosewood Drive, Danvers, MA 01923, (978) 750-8400.

The American College of Obstetricians and Gynecologists
409 12th Street, SW, PO Box 96920, Washington, DC 20090-6920

Premature rupture of membranes. Practice Bulletin No. 160. American College of Obstetricians and Gynecologists. *Obstet Gynecol* 2016; 127:e39–51.

