OBG MANAGEMENT

BY PATRICK DUFF, MD

Evaluation and management of preterm premature rupture of membranes

A simplified management algorithm—based on gestational age, fetal stability, and maternal infection—guides the clinician through the best options.

Management of preterm premature rupture of membranes (PPROM) is the most controversial of all obstetric problems. This article describes an algorithmic approach **(FIGURE)** to evaluation and treatment.

PPROM refers to rupture of membranes before onset of contractions at a gestational age less than 37 weeks. Approximately 30% to 40% of preterm deliveries are associated with PPROM.[1] In turn, preterm delivery is responsible for approximately 75% of all neonatal deaths, excluding infants with anomalies incompatible with life.[2]

PPROM is multifactorial and complex

PPROM may occur in patients with an incompetent cervix, which can result from previous genital tract surgery or laceration. PPROM occurs with increased frequency in women who smoke or who have multiple gestation, polyhydramnios, or antepartum hemorrhage. Some women with PPROM also appear to have inherent deficiencies in colla-

▪ *Dr. Duff is professor of obstetrics and gynecology, resident program director, and associate dean for student affairs, department of obstetrics and gynecology, division of maternal-fetal medicine, University of Florida College of Medicine, Gainesville, Fla.*

Evidence-based conclusions

The following conclusions are based on good and consistent evidence (level A recommendations) on management of patients with PPROM.

- As a rule, at a gestational age of less than 32 weeks, the greatest threat to the fetus is preterm delivery.
- If the gestational age is 32 weeks or more and fetal lung maturity is confirmed, the risks of expectant management usually exceed the risks of delivery.
- Outpatient management is appropriate only in a highly select group of women.
- In properly selected patients, the benefits of a single course of corticosteroids outweigh the risks.
- Tocolytics are effective in delaying delivery for 48 hours—a critical interval for the administration of corticosteroids.
- Prophylactic antibiotics prolong the latent period and reduce maternal and neonatal infection. These benefits clearly outweigh any risks such as allergic drug reaction or development of resistant organisms.

gen synthesis, which may predispose to weakening of the membranes.[1]

Infection link confirmed. Of greatest interest in recent years has been the confirmation that PPROM is associated with lower and upper genital tract infection; there are 3 major lines of supporting evidence:

- Many of the bacteria that inhabit the lower genital tract can produce phospholipase A, an enzyme that can trigger the arachidonic acid cascade that leads to the synthesis of prostaglandins. These same bacteria also are able to produce a variety of proteolytic enzymes that can degrade the collagen matrix of the chorioamniotic membranes.
- Compared to women with uncomplicated gestation, those with PPROM are more likely to have lower genital tract infections (such as group B streptococcal colonization or bacterial vaginosis).
- Compared to women with preterm labor and intact membranes, women with PPROM are more likely to have clinical and subclinical chorioamnionitis and inflammatory cytokines in the amniotic fluid.[2]

If the gestational age is less than 32 weeks and the mother and fetus are stable, expectant management is appropriate.

Direct observation is the best diagnostic test

Patients with PPROM usually note a sudden "gush" of fluid from the vagina. They also may experience a "constant leakage" of fluid or a sensation of "wetness" in the vagina or on the perineum.

The single best test to confirm the diagnosis is direct observation of amniotic fluid in the vaginal vault. Demonstration of severe oligohydramnios by ultrasound in a patient with a suggestive history also is helpful.

Although widely used, both the fern test and nitrazine test have pitfalls. The former may be falsely positive in the presence of highly estrogenized cervical mucus or extraneous saline on the glass side (e.g., from a fingerprint). The nitrazine test may be falsely positive in the presence of blood or seminal fluid.

Neonatal and maternal factors guide the management plan

The most important of several factors that must be considered in developing a management plan for PPROM are gestational age and availability of neonatal intensive care. For most patients at less than 36 weeks' gestation, the prudent course at a hospital with only a level 1 nursery is transfer to a tertiary care facility. If a level 2 nursery is available, the clinician may have sufficient support from neonatology staff to manage patients at 34 weeks' gestation.

Other important considerations include:

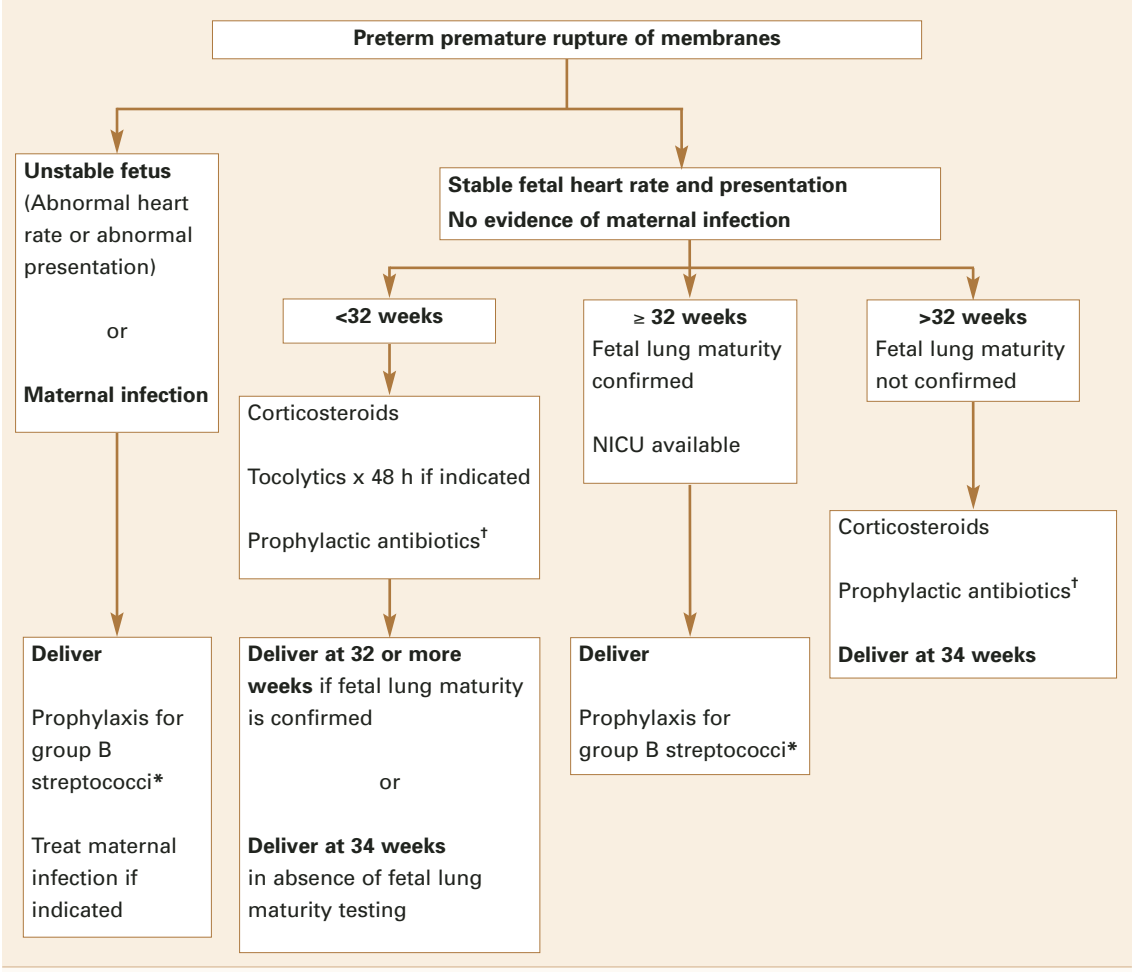
- the presence or absence of labor
- the presence of overt or subclinical infection,
- the stability of the fetal presentation and heart-rate tracing,
- the degree of fetal lung maturation, and
- the degree of cervical effacement and dilation.

The basic options for the patient with PPROM are expectant management or immediate delivery. Each poses potential complications for both mother and baby.

- **Expectant management.** The principal hazards are the risks of ascending infection, umbilical cord prolapse, umbilical cord compression due to oligohydramnios, and abruptio placentae.
- **Immediate delivery.** The major risks are the well-recognized complications of prematurity, including respiratory distress syndrome (RDS), intraventricular hemorrhage (IVH), sepsis, necrotizing enterocolitis (NEC), thermal instability, metabolic derangements, apnea and bradycardia, patent ductus arteriosus, and poor feeding. Of these, the 4 most likely to result in neonatal death are RDS, IVH, sepsis, and NEC, all of which are sig-

FIGURE

Management of preterm premature rupture of membranes



NICU = neonatal intensive care unit

***Prophylaxis for group B streptococci**
Penicillin: 5 million units intravenously (IV), then 2.5 million units IV every 4 h until delivery
or
Ampicillin: 2 g IV, then 1 g IV every 4 h

†Prophylactic antibiotics
Ampicillin: 2 g IV every 6 h x 48 h plus erythromycin: 250 mg IV every 6 h x 48 h then
Ampicillin: 500 mg by mouth every 6 h x 5 d or amoxicillin: 250 mg by mouth every 8 h x 5 d plus erythromycin base, 333 mg every 8 h x 5 d
(Azithromycin: 1,000 mg IV or by mouth, may be substituted for ampicillin/amoxicillin)

nificantly more likely at gestational ages below 32 weeks than at 32 weeks or more.

Algorithmic management approach

Assess stability of fetal presentation. After confirming the diagnosis of PPROM, the clinician should assess gestational age on the basis of history, physical examination, and ultrasound. The fetal presentation and estimated fetal weight should be determined, and the fetal heart rate should be monitored for evidence of recurrent variable decelerations.

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The mother should be evaluated for chorioamnionitis, primarily by assessment of temperature and maternal and fetal heart rate.

If the fetal presentation is unstable, thus predisposing to umbilical cord prolapse, or if the fetal heart rate tracing is worrisome, the patient should be delivered. If the gravida initially is admitted to a facility with only a level 1 nursery and maternal transfer is impractical, neonatal transfer should take place immediately after the birth.

Assess fetal lung maturity. At a gestational age of less than 32 weeks, lung maturity is very unlikely, and testing is not cost-effective. However, at 32 to 34 weeks, testing should be performed routinely. Amniotic fluid may be obtained by transabdominal amniocentesis or by aspiration of fluid pooled in the vaginal vault. Edwards et al[3] recently confirmed the reliability of this sampling method. Lung maturity may be assessed by means of the lecithin:sphingomyelin ratio, lamellar body count, or fetal lung maturity test.

If the fetal presentation is unstable or the fetal heart rate tracing is worrisome, the patient should be delivered.

The decision to deliver. If the gestational age is 32 weeks or more, fetal lung maturity is confirmed, and a neonatal intensive care unit is available, both mother and baby usually will fare better if delivered.

Patients should be treated intrapartum with antibiotics to prevent perinatal transmission of group B streptococcal infection. Appropriate regimens include penicillin, 5 million units intravenously (IV) initially, then 2.5 million units IV every 4 hours; or ampicillin, 2 g IV initially, then 1 g every 4 hours.

A recent study confirmed the value of this treatment plan.[4] In it, 164 patients at 32 to 36 weeks' gestation with confirmed fetal lung maturity were randomly assigned to delivery or expectant management. The mean gestational ages in the two groups were similar: 34.1 weeks in the former and 34.3 weeks in the latter group. The expectant management group had a longer duration of hospitalization for the mother and baby, and an increased rate of maternal infection and fetal heart rate abnormalities. In addition, the infants in this group received more frequent, prolonged antibiotic therapy.

Expectant management is appropriate for some patients. If gestational age is less than 32 weeks and the mother and fetus are stable, expectant management is appropriate.

If the patient is at 32 to 34 weeks' gestation and amniotic fluid cannot be obtained, she should be managed expectantly until 34 weeks. At 34 weeks, she should be delivered.

A recent study by Naef et al[5] confirmed the value of delivery at 34 weeks or more. In this investigation, 120 patients at 34 to 36 6/7 weeks' gestation were randomly assigned to oxytocin induction (n = 57) or expectant management (n = 63). Fetal lung maturity studies were not done. In the expectant management group, chorioamnionitis occurred more often (16% versus 2%, $P = .007$), maternal hospitalization was prolonged (5.2±6.8 days versus 2.6±1.6 days, $P = .006$), and there was a trend toward an increased rate of neonatal infection.

- **Corticosterioids.** A single course of corticosteroids should be administered to reduce the risk of neonatal RDS, IVH, and NEC.[2] Dosage regimens include 2 intramuscular (IM) doses of betamethasone, 12 mg, at 24-hour intervals, or 4 IM doses of dexamethasone, 6 mg, at 12-hour intervals. Tocolytics should be administered to delay delivery for 48 hours, thus permitting administration of corticosteroids.[3] Prolonged administration of tocolytics is not justified.
- **Testing for infection.** The patient should be tested for gonorrhea, chlamydia, bacterial vaginosis, and group B streptococcal colonization. If the test for bacterial vaginosis is positive, the patient should be treated with metronidazole, 250 mg orally, 3 times daily, for 7 days. If

gonorrhea is present, she should receive either cefixime, 400 mg orally in a single dose, or ceftriaxone, 125 mg IM in a single dose.[6]

The prophylactic antibiotics described here provide coverage for chlamydia and group B streptococci; nevertheless, testing for these organisms is indicated. If the patient tests positive for chlamydia, her partner must be notified and offered treatment. If the culture for group B streptococci is positive, the patient may require retreatment with antibiotics during labor.

■ **Prophylactic antibiotics**. Even in the absence of obvious lower genital tract infection, patients with PPROM benefit from antibiotic prophylaxis. Many studies investigating the role of prophylactic antibiotics in women with PPROM have been published.[7]

The largest and most strictly conducted trial was reported by Mercer et al[8] on behalf of the Maternal-Fetal Medicine Units Network. Participants—all women with PPROM between 24 and 32 weeks gestation—were randomly assigned to treatment with placebo or IV ampicillin plus erythromycin for 48 hours, followed by oral amoxicillin plus erythromycin for an additional 5 days. The main outcome measure was composite morbidity—at least 1 of the following complications: fetal or infant death, RDS, IVH, NEC, or sepsis within 72 hours of birth. (Researchers also looked at these morbidities individually.) Antibiotic prophylaxis significantly reduced the risk of composite morbidity (44.1% versus 52.9%, $P = .04$), RDS (40.5% versus 48.7%, $P = .04$), and NEC (2.3% versus 5.8%, $P = .03$). Among women who tested negative for group B streptococci, prophylactic antibiotics also significantly prolonged the latent period between PPROM and onset of labor ($P<.001$).

■ **Monitoring**. Patients selected for expectant management should be observed for evidence of maternal infection. Although a variety of laboratory tests have been proposed for the early diagnosis of infection (white blood cell count, C-reactive protein, nonstress test, biophysical profile, amniotic fluid glucose, or Gram stain), probably the most cost-effective method is monitoring maternal temperature and heart rate and fetal heart rate.

Patients also should be evaluated for signs of fetal cord compromise, best accomplished by serial nonstress tests. If signs of maternal infection or fetal compromise appear, delivery is indicated.

■ **Outpatient versus inpatient**. With rare exceptions, expectant management should take place in the hospital. Carlan et al[9] reported a randomized trial of outpatient management of PPROM, in which patients were included if they were judged to be compliant and met all of the following criteria: no evidence of cervical or intra-amniotic infection, minimal cervical dilation, stable fetal presentation, no sign of labor, reassuring heart-rate tracing, and easy access to the hospital. Patients initially were observed for 72 hours in the hospital.

Interestingly, only 67 of 349 patients (18%) fulfilled all criteria and therefore were considered for the trial. Compared to women who remained hospitalized, discharged patients hospital did not experience an increase in maternal infection or cesarean delivery rates. Infant outcomes also were similar. ■

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