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# Deliver or wait with late preterm membrane rupture?

While ACOG recommends delivery for all women with ruptured membranes after 34 weeks' gestation, a new study finds expectant management may be the way to go.

## PRACTICE CHANGER

In the absence of clinical indications for delivery, consider expectant management in women with premature rupture of membranes in late preterm stages (34 weeks to 36 weeks, 6 days).

## STRENGTH OF RECOMMENDATION

**B:** Based on one well-designed randomized controlled trial.<sup>1</sup>

Morris JM, Roberts CL, Bowen JR, et al; PPRoMT Collaboration. Immediate delivery compared with expectant management after preterm pre-labour rupture of the membranes close to term (PPRoMT trial): a randomised controlled trial. *Lancet*. 2016;387:444-452.

## ILLUSTRATIVE CASE

A 26-year-old G2P1001 at 35 weeks, 2 days of gestation presents with leakage of clear fluid for the last 2 hours. There is obvious pooling in the vaginal vault, and rupture of membranes is confirmed with appropriate testing. Her cervix is closed, she is not in labor, and tests of fetal well-being are reassuring. She had an uncomplicated vaginal delivery with her first child. How should you manage this situation?

**P**reterm premature rupture of membranes (PPROM)—when rupture of membranes occurs before 37 weeks' gestation—affects about 3% of all pregnancies in the United States, and is a major contributor to perinatal morbidity and mortality.<sup>2,3</sup> PPRoM management remains controversial, especially during the late preterm stage (ie, 34 weeks to 36 weeks, 6 days). Non-

reassuring fetal status, clinical chorioamnionitis, cord prolapse, and significant placental abruption are clear indications for delivery. In the absence of those factors, delivery vs expectant management is determined by gestational age. Between 23 and 34 weeks' gestation, when the fetus is at or close to viability, expectant management is recommended, provided there are no signs of infection or maternal or fetal compromise.<sup>4</sup> This is because of the significant morbidity and mortality associated with births before 34 weeks' gestation.<sup>4</sup>

The American College of Obstetricians and Gynecologists (ACOG) currently recommends delivery for all women with rupture of membranes after 34 weeks' gestation, while acknowledging that this recommendation is based on "limited and inconsistent scientific evidence."<sup>5</sup> The recommendation for delivery after 34 weeks is predicated on the belief that disability-free survival is high in late preterm infants. However, there is a growing body of evidence that shows negative short- and long-term effects for these children, including medical concerns, academic difficulties, and more frequent hospital admissions in early childhood.<sup>6,7</sup>

## STUDY SUMMARY

**Higher birth weights, fewer C-sections, and no increased sepsis with wait-and-see**  
The Preterm Pre-labour Rupture Of the Membranes close to Term (PPRoMT) trial was a

multicenter (65 institutions across 11 countries), randomized controlled trial (RCT) that included 1839 women with singleton pregnancies and confirmed rupture of membranes between 34 weeks and 36 weeks, 6 days' gestation.<sup>1</sup> Conducted from May 2004 to June 2013, participants were randomized to expectant management (915 women) vs immediate delivery by induction (924 women). Patients and care providers were not masked to treatment allocation, but those determining the primary outcome were masked to group allocation.

One woman in each group was lost to follow-up, and 2 additional women withdrew from the immediate birth group. Women already in active labor or with clinical indications for delivery (chorioamnionitis, abruption, cord prolapse, fetal distress) were excluded. The baseline characteristics of the 2 groups were similar.

Women in the induction group had delivery scheduled as soon as possible after randomization. Women in the expectant management group were allowed to go into spontaneous labor and were only induced if they reached term or the clinician identified other indications for immediate delivery.

The primary outcome was probable or confirmed neonatal sepsis. Secondary infant outcomes included a composite neonatal morbidity and mortality indicator (sepsis, mechanical ventilation  $\geq 24$  hours, still birth, or neonatal death), respiratory distress syndrome, any mechanical ventilation, birth weight, and duration of stay in a neonatal intensive care unit (NICU) or special care nursery. Secondary maternal outcomes included antepartum or intrapartum hemorrhage, intrapartum fever, mode of delivery, duration of hospital stay, and development of chorioamnionitis in the expectant management group.

The primary outcome of neonatal sepsis occurred in 2% of the neonates assigned to immediate delivery and 3% of neonates assigned to expectant management (relative risk [RR]=0.8; 95% confidence interval [CI], 0.5-1.3;  $P=.37$ ). There was also no statistically significant difference in composite neonatal morbidity and mortality (RR=1.2; 95% CI, 0.9-1.6;  $P=.32$ ). However, infants born in the immediate delivery group had

significantly lower birth weights (2574.7 g vs 2673.2 g; absolute difference= -125 g;  $P<.0001$ ), a higher incidence of respiratory distress (RR=1.6; 95% CI, 1.1-2.3;  $P=.008$ ; number needed to treat [NNT]=32), and spent more time in the NICU/special care nursery (4 days vs 2 days;  $P<.0001$ ).

Compared to immediate delivery, expectant management was associated with a higher likelihood of antepartum or intrapartum hemorrhage (RR=0.6; 95% CI, 0.4-0.9;  $P=.02$ ; number needed to harm [NNH]=50) and intrapartum fever (RR=0.4; 95% CI, 0.2-0.9;  $P=.02$ ; NNH=100). In the women assigned to immediate delivery, 26% had a cesarean section, compared to 19% in the expectant management group (RR=1.4; 95% CI, 1.2-1.7,  $P=.0001$ ; NNT=14). A total of 56 women (6%) assigned to the expectant management group developed clinically significant chorioamnionitis requiring delivery. All other secondary maternal and neonatal outcomes were equivalent with no significant differences between the 2 groups.

#### WHAT'S NEW?

##### Largest study to show no increased sepsis with expectant management

Two prior RCTs (the PPROMEXIL trial<sup>8</sup> and PPROMEXIL-2<sup>9</sup>), involving a total of 736 women, evaluated expectant management vs induction in the late preterm stage of pregnancy. There was no increased risk of neonatal sepsis with expectant management in either study. However, those studies did not have sufficient power to show a statistically significant change in any of the outcomes.

The PPROMT study is the largest one to show that immediate birth increases the risk of respiratory distress and duration of NICU/special care stay for the baby and increases the risk of cesarean section for the mother. It also showed that the risk of neonatal sepsis was not higher in the expectant management group.

#### CAVEATS

##### Findings only apply to singleton pregnancies

Delivery of the infants in the expectant management group was not by specified protocol;



**This study is the largest to show that immediate birth increases the risk of respiratory distress and duration of NICU stay.**

each birth was managed according to the policies of the local center and clinician judgment. Because of this, there was variation in fetal and maternal monitoring. The vast majority of women in both groups (92% to 93%) received intrapartum antibiotics. Expectant management should include careful monitoring for infection and hemorrhage and may need to be changed to immediate delivery if one of these occurs.

The study participants all had singleton pregnancies; this recommendation cannot be extended to non-singleton pregnancies. However, a prior cesarean section was not an exclusion criterion for the study, and these recommendations would be valid for that group of women, too.

**CHALLENGES TO IMPLEMENTATION**

**Going against the tide of ACOG**

The most recent ACOG guidelines, updated October 2016, recommend induction of labor for women with ruptured membranes in the late preterm stages.<sup>5</sup> This may present a challenge to widespread acceptance of expectant management for PPROM. **JFP**

**ACKNOWLEDGEMENT**

The PURLs Surveillance System was supported in part by Grant Number UL1RR024999 from the National Center For Research

Resources, a Clinical Translational Science Award to the University of Chicago. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Center For Research Resources or the National Institutes of Health.

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