Preterm Premature Rupture of Membranes

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Clinical Case

- 29 y/o G1P0 presents at 31+3 weeks complaining of a sudden "gush" of fluid while standing at work today.
- **HCP**
  - EDD 11/27/2016 by LMP
  - Threatened abortion at 12 weeks
  - Symptomatic bacterial vaginosis treated with clindamycin at ~24 weeks
  - Tobacco use throughout pregnancy
  - Ultrasound at 20 weeks showed no abnormalities
  - PNL: O+, Ab neg, rubella immune, HBsAg NR, HIV NR, RPR NR, GCT 120 mg/dL, GBS unknown

Clinical Case – cont'd

- **Gyn Hx**: symptomatic BV at 24 weeks, tx'd with clindamycin
- **PMH**: none
- **PSH**: none
- **Meds**: PNV
- **Allergies**: NKDA
- **SH**: 10 pack year smoking history, cont'd throughout pregnancy. No other drug or alcohol use.
- **FH**: noncontributory

Clinical Case – cont'd

- + pooling, + nitrazine, + ferning
- **SVE**: deferred
- **SSE**: 2cm dilated
- **EFM**: baseline 150s, moderate variability, + accels, no decels
- **Tocometry**: no contractions
- **BSUS**: vertex, S == D, AFI 5.0

Objectives

- **Definition and Background**
- Expected Clinical Course
- Management and Delivery

Definition & Epidemiology

- Rupture of membranes (**ROM**) occurs due to:
  - Increased apoptosis
  - Increased collagenase activity
  - Shearing forces from uterine contractions
- **Preterm Premature ROM (PPROM)**: membrane rupture before the onset of uterine contractions **and** [23+0/7 - 37+0) weeks of gestation
- Common pathologic causes include **intrauterine infection**, **mechanical stretching**, and **placental abruption**.
- ~3% of all pregnancies
  - Responsible for approx. 1/3 of all preterm births

Risk Factors

Maternal Factors	
	PPROM in prior pregnancy
	Antepartum vaginal bleeding
	Collagen/vascular disorders (e.g. Ehlers-Danlos, SLE)
	Direct abdominal trauma
	Cigarette smoking
	Low BMI (BMI < 19.8 kg/m^2)
Uteroplacental Factors	
	Uterine anomalies (e.g. uterine septum)
	Placental abruption
	Prior cervical conization
	Uterine overdistention (polyhydramnios, multiple pregnancy)
	Intra-amniotic infection/chorioamnionitis

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Maternal Risks

- Chorioamnionitis (cause or complication): 13-60%
- Postpartum Endometritis: 2-13%
- Placental Abruption: 4-12%
- Retained placenta or postpartum hemorrhage: 12%

Fetal Risks

- Overall risk of morbidity and mortality is mostly dependent on gestational age.
  - Neonatal sepsis, meningitis, pulmonary hypoplasia, and neurological sequelae are all "common" complications of preterm delivery.
- Malpresentation and cord prolapse (11%)
- PPROM with preterm delivery vs. preterm delivery without PPROM – relative risk of neonatal infection is ~2

Clinical Course

- **Latent Period** = time from membrane rupture to delivery.
- **Prophylactic antibiotics** are standard and have been shown to significantly increase the latent period (e.g. 2.9 vs 6.1 days) and reduce certain perinatal morbidities..

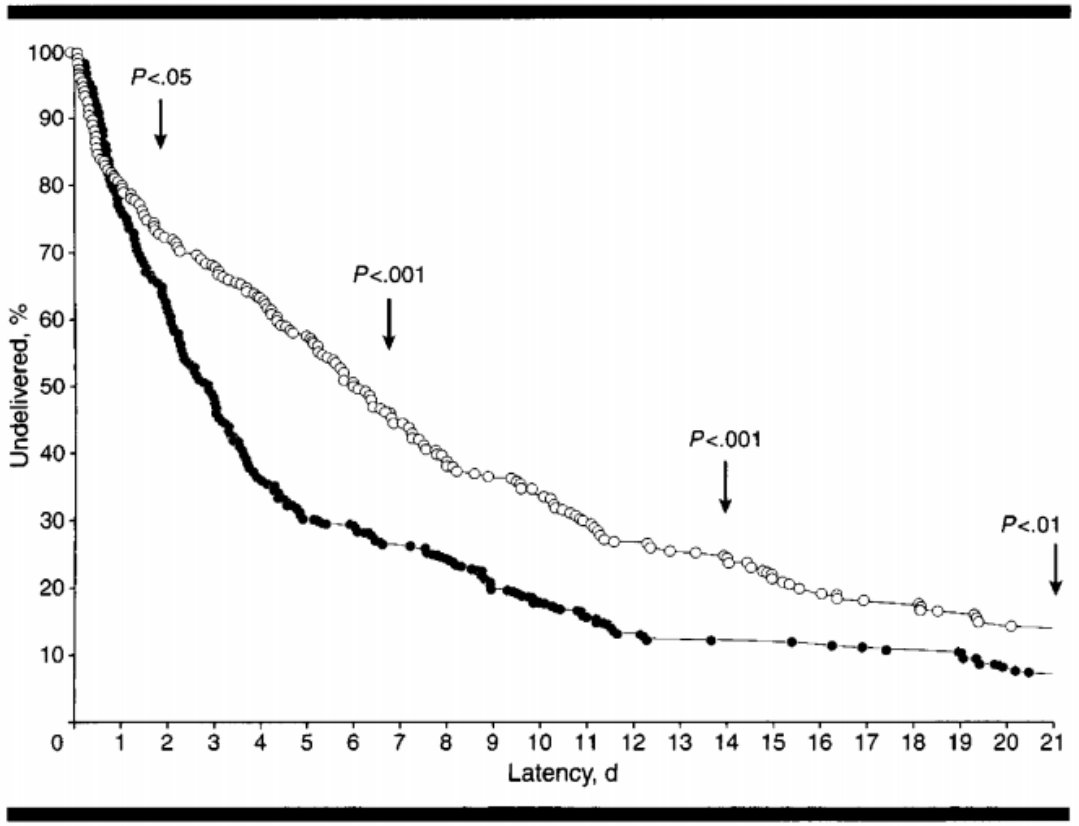


Figure 2.—Interval from randomization to delivery after expectant management of preterm premature rupture of the membranes at 24 weeks' and 0 days' gestation to 32 weeks' and 0 days' gestation according to antibiotic-group or placebo-group assignment. The *P* values reflect analysis of percentage of women whose neonates remained undelivered. For the survival analysis, $P<.001$.

(Mercer, et al. 1997)

Objectives

- Definition and Background
- Expected Clinical Course
- **Management and Delivery**

Management – Initial Approach

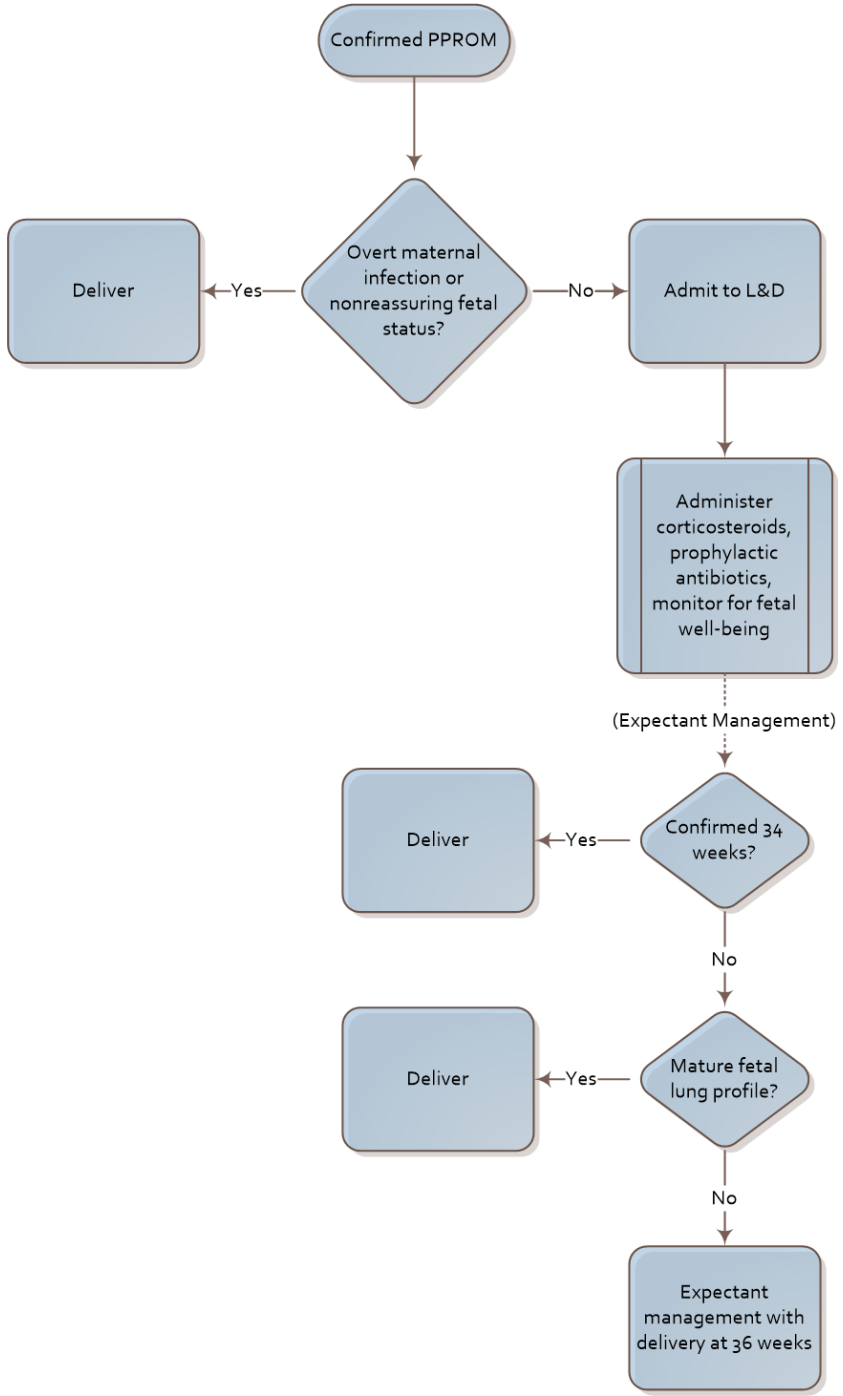
- Sterile speculum exam to:
  - Assess likelihood of vaginal infection
  - Obtain cultures
  - Obtain fluid for nitrazine/fern/other testing
  - Visualize dilation of cervix
- **Confirmation** of PPROM
  - Pooling, +nitrazine, +ferning
  - Amnisure (99% sensitivity & specificity) – but *expensive*
- **Avoid** digital cervical exam (decreases latent period by average of 2 days)
- Ultrasound exam of fetus for growth, position, residual amniotic fluid, fetal anatomy

Management – Further Testing

- CBC
- Rectovaginal GBS cultures
- EFM and tocometry
- Gonorrhoeae and Chlamydia NAAT
- Lamellar body count/lecithin:sphingomyelin ratio (if indicated)

Management

- Admit to the hospital for observation.
- First decision: induce labor/cesarean vs. manage expectantly.



What to Expect When You're Expectantly Managing PPROM

- **Antenatal corticosteroids**: 2015 Cochrane Review supports use between 23 – 34 weeks gestation
  - *Decreased* respiratory distress syndrome (RR 0.83, CI 0.75-0.91), composite of intraventricular hemorrhage, necrotizing enterocolitis, duration of neonatal respiratory support (RR 0.84, CI 0.75-0.94).
  - *No difference* in early childhood follow-up for total deaths, survival free of disability, disability.
- **Antibiotic Prophylaxis**: 2013 Cochrane Review supports 7 day course for any PPROM < 37 weeks.
  - *Decreased* need for surfactant, neonatal O2 therapy, neonatal and maternal infections.
  - *Increased* the latent period.
  - *No change* in perinatal mortality.

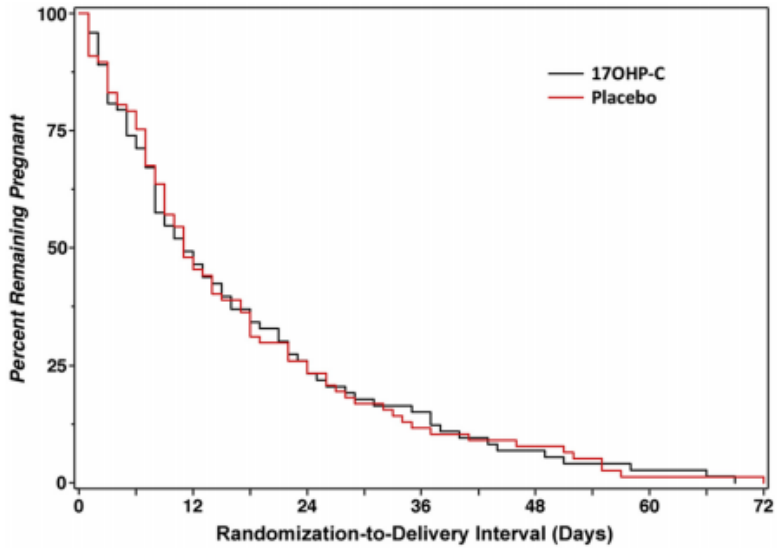
What to Expect When You're Expectantly Managing PPROM – cont'd

- **Tocolysis**: 2014 Cochrane Review found insufficient evidence to support/refute use of tocolysis in PPROM.
  - *Increased* latent period (mean difference 73hrs), incidence of 5 min Apgars < 7 ((RR 6.05; 95% CI 1.65 to 22.23), incidence of chorioamnionitis in mothers with PPROM < 34 weeks.
  - *No change* in maternal/neonatal outcomes (e.g. perinatal mortality [RR 1.67, CI 0.85-3.29], trial of 402 births).

What to Expect When You're Expectantly Managing PPROM – cont'd

- **Supplemental Progesterone**: 2015 multicenter RCT did not support use of supplemental progesterone in PPROM.
  - *No change* in pregnancy length or perinatal morbidity.

FIGURE 2
Randomization-to-delivery interval in the 2 groups



Randomization-to-delivery interval was not significantly different between the groups ($P = .62$, Cox regression adjusted for gestational age at randomization).

17OHP-C, 17-hydroxyprogesterone caproate.

Combs. 17-hydroxyprogesterone caproate for PROM. Am J Obstet Gynecol 2015.

TABLE 3
Secondary perinatal efficacy outcomes

Variable	Group: 17-hydroxyprogesterone caproate (n = 73)	Placebo (n = 77)	*P* value
Composite adverse perinatal outcome, n (%)	46 (63)	49 (64)	.64[a]
Components of the composite, n (%)			
Stillbirth	0	0	NA
Neonatal death[b]	3 (4)	2 (3)	.67[c]
Infant death[d] before hospital discharge	0	0	NA
Respiratory distress syndrome	44 (60)	46 (60)	.72[a]
Intraventricular hemorrhage, grade 3 or 4	1 (1)	1 (1)	1.00[c]
Necrotizing enterocolitis, stage 2 or 3	3 (4)	2 (3)	.67[c]
Sepsis within 72 hours of birth	3 (4)	1 (1)	.36[c]
Periventricular leukomalacia	1 (1)	2 (3)	1.00[c]

[a] Cochran-Mantel-Haenszel χ^2 stratified by gestational age at randomization; [b] Death at ≤28 days of life; [c] Fisher exact test, unadjusted because of the small number of events; [d] Death at 29-60 days of life.

Combs. 17-hydroxyprogesterone caproate for PROM. Am J Obstet Gynecol 2015.

Delivery after PPROM

- **Fetal lung maturity**: consider testing after 34 weeks if the gestational age of the pregnancy is in doubt.
- **Magnesium sulfate** is administered as standard for pregnancies [24 – 32) weeks, for fetal neuroprotection.
  - E.g. decreased cerebral palsy (RR 0.68, CI 0.54 – 0.87, 6145 infants)
- **Misoprostol** or **oxytocin** may be used.
  - Avoid "mechanical" methods of cervical ripening due to foreign body infection risk.
- **Cesarean section** is performed only for standard indications.
  - Most PPROM mothers will deliver vaginally.

Returning to the Clinical Case…

Clinical Case – Follow-up

- 29 y/o G1P0 with PPROM at 31+3 weeks is admitted to L&D. After evaluation, the fetal wellbeing is found to be reassuring and the mother does not exhibit any signs of chorioamnionitis.
- The patient is expectantly managed with antenatal corticosteroids and prophylactic antibiotics, and she has a normal spontaneous vaginal delivery at 32+3 weeks.

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