The case for amniocentesis for fetal lung maturity in late-preterm and early-term gestations

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The recent American College of Obstetricians and Gynecologists Committee Opinion no. 560 and the Society of Maternal-Fetal Medicine article argue for the abandonment of fetal lung maturity (FLM) testing.[1,2] We concur with the conclusion that the timing of delivery in certain complicated obstetric conditions can be complex and that a risk management decision must be made. This process involves considering the risks to the neonate from premature birth vs maternal and fetal risks that are associated with pregnancy continuation. Neonatal risks to late-preterm and early-term delivery that can be relatively minor and not result in any significant increased risk for long-term disability include temperature instability, poor or slow feeding, hyperbilirubinemia, hypoglycemia, and transient tachypnea of the newborn infant. Neonatal risks that can be major include intubation with surfactant deficient hyaline membrane disease, necrotizing enterocolitis, and intraventricular hemorrhage. Conversely, the risks to the mother with pregnancy continuation can include significant hemorrhage with a placenta previa, seizures or the development of HELLP (hemolysis, elevated liver enzymes, and low platelet count) syndrome in patients with preeclampsia, uterine rupture in patients with previous classic cesarean delivery, and others. The fetal risks with pregnancy continuation can include intrauterine stillbirth or hypoxic ischemic injury that leads to neurologic damage.

We do not agree, however, with the statement "amniocentesis for the determination of fetal lung maturity in well-dated pregnancies generally should not be used to guide the timing of delivery." We concur that if a clear indication for a late-preterm or early-term delivery exists, such as severe preeclampsia, then delivery should occur regardless of FLM testing. However, we have concern with the statement, "if delivery could be safely delayed in the context of an immature lung profile result then no clear indication for late-preterm or early-term delivery actually exists." There are many situations in which there are no black or white decisions to deliver or to manage expectantly. Furthermore, there are numerous cases in which, although delivery may seem a reasonable option in view of the danger to mother or fetus with continuing the pregnancy, knowing that the fetus will have a rocky course as a neonate will cause the clinician to delay delivery with careful antenatal monitoring of the mother and fetus in the interim. This is where clinicians can use FLM testing to further help in the decision-making process.

One of the arguments against FLM testing is that the result does not predict that all organ systems of the fetus are ready for after-birth life. To clarify, however, FLM testing was developed to prove that the fetal lungs are mature and that the risk of intubation for surfactant deficient hyaline membrane disease is minimal at $\leq$1%.[3] The risk of major neonatal complications, such as intraventricular hemorrhage and necrotizing enterocolitis, is small at $\geq$34 0/7 weeks' gestation, but the risk is not zero, and most of these complications occur in newborn infants who are intubated.[4,5]

The studies of Bates et al[6] and Kamath et al[7] that argue no benefit to FLM testing have patients that were not comparable. The subjects in those studies who had an amniocentesis in most cases underwent the procedure because something was potentially not normal or was concerning to the clinician. This group of patients was then compared with a group that delivered spontaneously after 39 weeks' gestation. These 2 groups of patients are not equal. To truly answer the question, a multicenter study would need to be performed on a large group of complicated obstetrics patients who are late-preterm or early-term whereby randomization to delivery vs amniocentesis to guide management is performed. This could maximize the likelihood that the 2 groups would have a similar risk. Furthermore, although surfactant deficient hyaline membrane disease is less common in the late-preterm or early-term gestation, research has not fully answered whether corticosteroids are beneficial if administered to this gestational age group in the presence of an immature lung profile; however, 2 studies do suggest that there could be a benefit.[8,9] It is conceivable that the best management approach, if a large enough study could be performed, would be to recommend amniocentesis in complicated late-preterm or early-term pregnancies with delivery after a mature FLM test result and corticosteroids followed by delivery with an immature FLM test result.

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To elaborate further, let us use a 38-year-old pregnant patient with difficult-to-control chronic hypertension. The "suggested" time for delivery without amniocentesis based on the ACOG Committee Opinion is 36 0/7 to 37 6/7 weeks' gestation. To begin, what is the definition of "difficult-to-control chronic hypertension"? If we ignore this question, one option a clinician might choose is to deliver at 36 0/7 weeks' gestation, thereby taking the risk of the newborn infant being admitted to the neonatal intensive care unit (NICU) intubated with surfactant deficient hyaline membrane disease. The alternate option would be to wait another 7-13 days that has the risk of stillbirth or placental abruption, which could lead to maternal hemorrhage and fetal compromise. In a 38-year-old pregnant patient with difficult-to-control chronic hypertension, what is the risk of stillbirth and placental abruption in the 13 days between 36 0/7 and 37 6/7 weeks' gestation? Additionally, what is the real risk of stillbirth with carefully used antepartum biophysical profile and nonstress testing? One can only make this decision when the other side of the equation is known; gestational age and fetal growth alone do not give the clinician as accurate a picture as can be known.

An FLM amniocentesis in this setting and many other obstetric conditions can help guide the management decision process. If the FLM test is mature, the risk benefit analysis is that the risk to the neonate of severe morbidity is $\leq$1%, and the risk for NICU admission for minor morbidity might be 5-10% vs some unknown risk with waiting. Conversely, if the test is immature, the risk of NICU admission for more severe neonatal morbidity could be $\geq$20%.[10,11] Without FLM testing, a clinician is left with only an educated guess as to whether it is better to deliver without testing at 36 0/7 weeks or to wait another week or 2.

To conclude, we strongly urge that the use of FLM testing not be abandoned in selected late-preterm and early-term pregnancies for which the decision to deliver or to buy more time is in the gray zone and not as clear cut as recent statements and publications have made them out to be. ■

REFERENCES

1. American College of Obstetricians and Gynecologists. ACOG Committee opinion no. 560. Medically indicated late-preterm and early-term deliveries. Obstet Gynecol 2013;121:908-10.

2. Spong CY, Mercer BM, D'Alton M, Kilpatrick S, Blackwell S, Saade G. Timing of indicated late-preterm and early-term birth. Obstet Gynecol 2011;118:323-33.

3. Gluck L, Kulovich MV, Borer RC Jr, Brenner PH, Anderson GG, Spellacy WN. Diagnosis of the respiratory distress syndrome by amniocentesis. Am J Obstet Gynecol 1971;109:440-5.

4. Clark RH, Gordon P, Walker WM, Laughon M, Smith PB, Spitzer AR. Characteristics of patients who die of necrotizing enterocolitis. J Perinatol 2011;32:199-204.

5. Thorp JA, Jones PG, Clark RH, Knox E, Peabody JL. Perinatal factors associated with severe intracranial hemorrhage. Am J Obstet Gynecol 2001;185:859-62.

6. Bates E, Rouse DJ, Mann ML, Chapman V, Carlo WA, Tita ATN. Neonatal outcomes after demonstrated fetal lung maturity before 39 weeks of gestation. Obstet Gynecol 2010;116:1288-95.

7. Kamath BD, Marcotte MP, DeFranco EA. Neonatal morbidity after documented fetal lung maturity in late preterm and early term infants. Am J Obstet Gynecol 2011;204:518.e1-8.

8. Yinon Y, Haas J, Mazaki-Tovi S, et al. Should patients with documented fetal lung immaturity after 34 weeks of gestation be treated with steroids? Am J Obstet Gynecol 2012;207:222.e1-4.

9. Shanks A, Gross G, Shim T, Allsworth J, Sadovsky Y, Bildirici I. Administration of steroids after 34 weeks of gestation enhances fetal lung maturity profiles. Am J Obstet Gynecol 2010;203:47.e1-5.

10. Neerhof MG, Haney EI, Silver RK, Ashwood ER, Lee I-S, Piazze JJ. Lamellar body counts compared with traditional phospholipid analysis as an assay for evaluating fetal lung maturity. Obstet Gynecol 2001;97:305-9.

11. Karcher R, Sykes E, Batton D, et al. Gestational age-specific predicted risk of neonatal respiratory distress syndrome using lamellar body count and surfactant-to-albumin ratio in amniotic fluid. Am J Obstet Gynecol 2005;193:1680-4.