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Short Communication

End of the line for fetal lung maturity testing

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ABSTRACT

Objective: During the last decade, guidelines published by the American College of Obstetricians and Gynecologists (ACOG) and Society for Maternal Fetal Medicine (SMFM) have emphasized an increasingly limited role for fetal lung maturity (FLM) testing. As a reference laboratory for FLM testing, we were therefore interested in determining the impact of changing guidelines on our test volumes.

Methods: We retrospectively reviewed FLM test volume data from 2006 to 2016 for the following FLM assays: lecithin/sphingomyelin ratio, phosphatidylglycerol, disaturated lecithin, and lamellar body count.

Results: We found that there was a precipitous decline in test volumes from 2006 to 2016; our analysis led us to discontinue providing reference laboratory FLM testing in 2016 given the very low volumes.

Conclusions: The 2019 ACOG guidelines now state that FLM testing no longer has clinical utility. Therefore, clinical laboratory directors should meet with obstetrics providers to discuss discontinuation of FLM testing at their institutions.

1. Introduction

Fetal lung maturity (FLM) testing, first developed in 1971 by Gluck et al. [1], has been utilized over the years to assess the potential risk for development of respiratory distress syndrome (RDS). In theory, FLM assays should be able to predict if a fetus is at risk for RDS. In practice, studies found that the positive predictive value, or ability of FLM tests to predict immature fetal lungs, was poor (~20–50%) [2]. However, the negative predictive value, or ability of FLM tests to predict mature fetal lungs, was previously thought to be acceptable (~95–100%) [2]. Unfortunately, a more detailed analysis of the negative predictive value showed that it changes with gestational age [3]. Additionally, gestational age alone may be the best estimator of risk for RDS. Thus, the clinical utility of FLM assays has been largely debated.

The American College of Obstetricians and Gynecologists (ACOG) has provided guidance to clinicians regarding the utility of FLM testing. Table 1 provides a summary of the guidelines for FLM testing from several ACOG practice bulletins and committee opinions, usually in partnership with the Society for Maternal Fetal Medicine (SMFM) [2,4–9]. During the last decade the guidelines have emphasized an increasingly limited role for FLM testing.

The University of Minnesota Medical Center (UMMC) has served as a reference laboratory for FLM testing since 1975, performing thin layer chromatography (TLC) quantitation of amniotic fluid lecithin/sphingomyelin ratio (L/S), phosphatidylglycerol (PG), and disaturated lecithin (DSL). UMMC switched from the laborious TLC methods to lamellar body count (LBC) in 2013. Given the emphasis on decreasing utility for FLM testing in ACOG guidelines, we were interested in retrospectively looking at our test volumes to determine the impact of the ACOG guidelines on FLM test ordering practices.

2. Methods

Our laboratory information system was queried from 2006 to 2016 for terms associated with FLM testing: lecithin/sphingomyelin ratio (L/S), phosphatidylglycerol (PG), disaturated lecithin (DSL), and lamellar body count (LBC). The TLC assays were performed from 1975 to 2015, and the LBC assay from 2013 to 2016. The LBC assay was validated on our hematology platform, the Sysmex XE 5000. Clinicians likely ordered DSL, L/S, and PG for a single patient, but we did not confirm this with chart reviews.

Abbreviations: FLM, fetal lung maturity; RDS, respiratory distress syndrome; ACOG, American College of Obstetricians and Gynecologists; SMFM, Society for Maternal Fetal Medicine; TLC, thin layer chromatography; L/S, lecithin/sphingomyelin ratio; PG, phosphatidylglycerol; DSL, disaturated lecithin; LBC, lamellar body count; UMMC, University of Minnesota Medical Center; SOGC, Society of Obstetrics and Gynecologists of Canada

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Table 1
Summary of guidance related to FLM testing from ACOG and SMFM practice bulletins and committee opinions [2,4–9].

Year	Number*	Title	Summary concerning FLM testing
2008	97	Fetal lung maturity [2]	Consider FLM testing for poorly dated pregnancies.
2009	107	Induction of labor [4]	
2013	560	Medically indicated late-preterm and early-term deliveries [5]	FLM testing should not be used in well-dated pregnancies.
2013	561	Non-medically indicated early-term deliveries [6]	Documentation of FLM testing does not justify early delivery. Other factors related to the mother and fetus should be considered.
2017	688	Management of suboptimally dated pregnancies [7]	FLM testing is not recommended as a component for the decision making process for delivery, even in suboptimally dated pregnancies.
2019	764	Medically indicated late-preterm and early-term deliveries [9]	If there is a medical indication for delivery, then delivery should occur regardless of FLM testing.
2019	765	Avoidance of nonmedically indicated early-term deliveries and associated neonatal morbidities. [8]	FLM testing is not recommended to guide timing of delivery, even in suboptimally dated pregnancies.

Number* refers to the committee opinion number or practice bulletin number issued by ACOG.

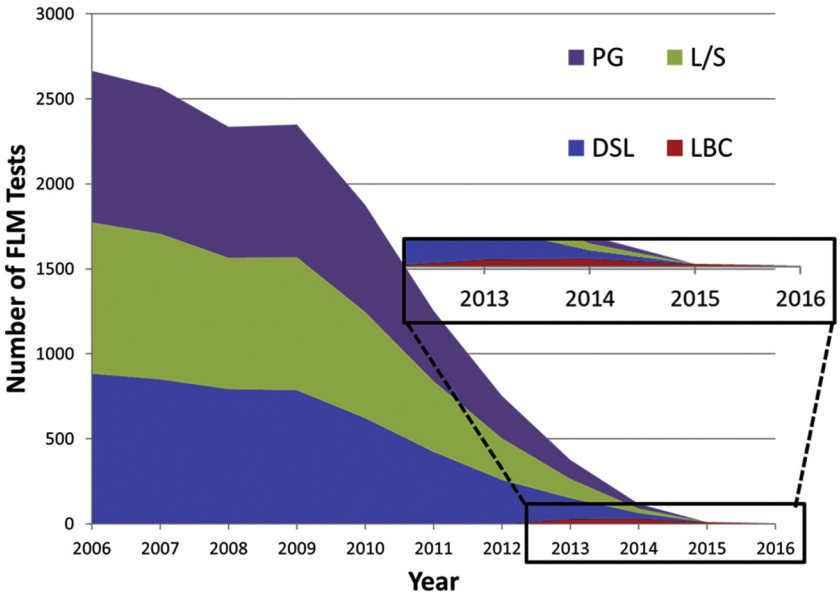

Fig. 1. Cumulative total of FLM tests per year at UMMC from 2006 to 2016. Lecithin/sphingomyelin ratio (L/S), phosphatidylglycerol (PG), disaturated lecithin (DSL), and lamellar body count (LBC).

3. Results

UMMC observed a precipitous decline in FLM testing from 2006 to 2016 (Fig. 1). The TLC assays were the preferred method for our institution, with a peak volume in 2006 of 2665 test results split across the three tests (884 DSL, 891 L/S ratio, and 890 PG). Since the process of performing the TLC assays was both time consuming and laborious, we switched to the LBC in 2013. The LBC assay had a peak volume in 2014 of 29 test results.

4. Discussion

As of 2019, the ACOG and SMFM guidelines advise clinicians against using FLM test results in the decision to deliver, for all pregnancy scenarios: well-dated pregnancies [5], suboptimally dated pregnancies [7], non-medically indicated early pregnancies [6,8], and medically indicated early pregnancies [9] (see Table 1). As ACOG and SMFM addressed in several practice bulletins, studies have found that even with a mature FLM result, the neonate is still at risk for complications related to early term birth [10,11]. Tita et al. found that outcome measures such as continuous positive airway pressure (CPAP) and hyperbilirubinemia requiring phototherapy were significantly increased in non-medically indicated early term births (37^0–38^6 weeks) with FLM test results suggestive of mature lungs [10]. Additionally, Bates et al. found that neonates delivered at 36–38 weeks gestational age were at increased risk for RDS, hyperbilirubinemia, and hypoglycemia despite mature FLM results [11]. Therefore, the decision to deliver should be more broadly based on multiple maternal and fetal parameters, and not just the fetal lung status. Citing these studies, ACOG and SMFM guidelines have advised clinicians to discontinue the practice of performing amniocentesis for the sole purpose of FLM testing since the result should not be used in the decision to deliver [8,9].

Based on literature, the decline in FLM testing likely began in the 1990's [12]. One study that surveyed SMFM fellows found that many clinicians felt that the FLM result was not needed for patient care [12]. Although we do not have data prior to 2006, our data supports the steady downward trend for FLM testing noted in the literature (Fig. 1) [3,13]. Our data also shows the end of the decline, since FLM testing was discontinued in 2016 at our institution.

The downward trend for FLM testing is likely due to several reasons. First, as mentioned previously, the ACOG and SMFM recommendations highlighted important studies that demonstrated FLM results should not be used in the clinical decision for delivery because they are unreliable in predicting the overall health outcomes of the neonate and mother (Table 1, [8,9]). Second, both societies have recommended that clinicians reduce non-medically indicated early term deliveries, reducing preterm births in general in the US [3]. Third, the practice of estimating due date by ultrasound has become more accurate and standardized. Thus, clinicians can estimate the risk for RDS and other complications

based on gestational age. Lastly, there are better treatment options such as antenatal corticosteroids [14], ventilators/CPAP for infants, and artificial surfactants to decrease surface tension in infant lungs [15].

Both Canadian and European guidelines have largely focused on treatment of RDS, rather than FLM testing. The Society of Obstetrics and Gynecologists of Canada (SOGC) recently updated guidelines regarding use of antenatal corticosteroid therapy [14]. The guidelines emphasized the balance between the benefit of steroids in reducing perinatal morbidity from a variety of complications, including RDS, with the risk for maternal morbidity from infection and adrenal suppression. The European consensus guidelines on the management of respiratory distress have been updated every three years since 2007 to highlight advancements in technology and treatment options for neonates suffering from RDS [15]. There is a single sentence in the European guidelines published in 2019 regarding FLM testing which states: "In some cases when an early CS [C-section] is needed, establishment of fetal lung maturity may be better than giving steroids to all women." However, this recommendation is not mentioned in either the ACOG or SOGC guidelines, and there are no published studies demonstrating better outcomes when FLM testing is performed instead of administering steroid therapy.

In conclusion, current research and recommendations argue against amniocentesis for FLM testing to guide the decision for delivery in any clinical situation of pregnancy. Clinicians now have better tools and information to support the neonate and mother for both early (medically indicated) and full-term births. Given the changing clinical landscape, clinical laboratory directors should meet with obstetrics providers to discuss discontinuation of FLM testing.

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