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C58-A

Assessment of Fetal Lung Maturity by the Lamellar Body Count; Approved Guideline

This document provides guidelines for the use of automated cell counting to enumerate lamellar bodies in amniotic fluid. It describes the different counting technologies used in automated cell counters as well as methods laboratorians can use to verify/validate the lamellar body count test.

A guideline for global application developed through the Clinical and Laboratory Standards Institute consensus process.

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Assessment of Fetal Lung Maturity by the Lamellar Body Count; Approved Guideline

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Abstract

Clinical and Laboratory Standards Institute document C58-A—*Assessment of Fetal Lung Maturity by the Lamellar Body Count; Approved Guideline* provides guidance to laboratory professionals and manufacturers involved in the development of devices and materials related to the enumeration of lamellar bodies in amniotic fluid as a test of fetal lung maturity (FLM). Physicians use FLM tests to weigh the potential risks to a newborn of developing respiratory distress syndrome caused by a deficiency of pulmonary surfactant. Pulmonary surfactant decreases the surface tension of the hydrated inner layer of alveoli and prevents their collapse during exhalation. Pulmonary surfactant is packaged into lamellar bodies that are secreted from pneumocytes. The enumeration of lamellar bodies in amniotic fluid can be used as a test of FLM. This document provides guidelines for the use of automated cell counting to perform the lamellar body count test and describes methods to assist in test verification and validation.

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Foreword

Development of the fetal lung can be divided into four stages: the pseudoglandular, canalicular, saccular, and alveolar stages. The first stage results in the development of three lung lobes on the right side and two on the left side.[1] The second stage is remarkable for the differentiation of type I and type II pneumocytes and the first appearance of surfactant. The third stage involves formation of clusters of wide spaces in the peripheral airways. Finally, the fourth stage involves the formation of alveoli. It is during this stage that type II pneumocytes increase production of pulmonary surfactant. Lung development continues for approximately eight years.

Pulmonary surfactant functions to coat the alveolar epithelium and decrease the surface tension of the hydrated inner layer of alveoli. When surface tension is high and the alveolar radius is small, very high air pressure is needed to prevent alveolar collapse. Surfactant decreases the air pressure required to keep the alveoli from collapsing. Surfactant is composed of approximately 90% phospholipid and 10% protein, and is packaged into layered storage granules called lamellar bodies that begin to synthesize around 24 weeks of gestation. Lamellar bodies are secreted by the type II pneumocyte and unfold to form tubular myelin and other large aggregates that are adsorbed onto the hydrated inner layer of the alveoli.

Respiratory distress syndrome (RDS) in premature infants is caused by developmental insufficiency of pulmonary surfactant production and structural immaturity of the lungs. Clinically, RDS presents with hypoxia, hypercapnia, and acidosis. Preventing premature birth is the most effective way to prevent RDS. Alternatively, administration of steroids to the mother can be used to accelerate lung surfactant production. Treatment of preterm newborns after birth with exogenous surfactant can be effective in preventing and treating RDS.

Fetal lung maturity (FLM) tests are used by physicians to weigh the risk of developing RDS if the newborn is delivered against the risk to the mother by continuing the gestation. To be clinically useful, FLM tests should possess high diagnostic sensitivity for RDS and a high predictive value of a mature result. Interestingly, no studies have addressed the impact of FLM testing on improving patient care. Studies have indicated that the frequency of physician-ordered FLM testing is decreasing.[2,3] This likely reflects a decrease in elective deliveries in response to studies that demonstrate more adverse outcomes in infants delivered before 39 weeks of gestation.[4,5] However, despite the decreased use of FLM tests, physicians still report that they rely on them for clinical decision making.[3]

Key Words

Amniotic fluid, fetal lung maturity, lamellar bodies, lamellar body count, respiratory distress syndrome

Assessment of Fetal Lung Maturity by the Lamellar Body Count; Approved Guideline

1 Scope

This document provides guidelines for the use of automated cell counting to enumerate lamellar bodies in amniotic fluid. It describes the different counting technologies used in automated cell counters as well as methods laboratorians can use to verify/validate the lamellar body count (LBC) test.

The intended users of this guideline are laboratory directors, medical technologists, laboratory supervisors, and pathologists, as well as *in vitro* diagnostic manufacturers involved in the development of devices and materials related to LBC testing.

This guideline does not provide guidance on how to establish the clinical utility of the LBC for fetal lung maturity (FLM).

2 Introduction

In 1988, Stuart Dubin used light scattering to study the refractive index of amniotic fluid as a measure of FLM.[6,7] His observations led to the determination of the lamellar body number density (lamellar bodies per unit volume; typically between 10 000 and 200 000/µL) and demonstrated that lamellar bodies are similar in size to platelets (1.7–7.3 fL or 1–5 µm vs 5–7 fL or 2–4 µm, respectively). The latter finding suggested that lamellar bodies could be quantified using the platelet channel of an automated cell counter.

Since those early observations, lamellar body counting has proven to have many advantages over other tests of FLM, including:

- Rapid turnaround time
- Low reagent cost
- Wide availability
- Low degree of technical difficulty
- Low volume of amniotic fluid required
- Excellent clinical performance

3 Standard Precautions

Because it is often impossible to know what isolates or specimens might be infectious, all patient and laboratory specimens are treated as infectious and handled according to “standard precautions.” Standard precautions are guidelines that combine the major features of “universal precautions and body substance isolation” practices. Standard precautions cover the transmission of all known infectious agents and thus are more comprehensive than universal precautions, which are intended to apply only to transmission of blood-borne pathogens. Standard and universal precaution guidelines are available from the Centers for Disease Control and Prevention.[8] For specific precautions for preventing the laboratory transmission of all known infectious agents from laboratory instruments and materials and for recommendations for the management of exposure to all known infectious diseases, refer to CLSI document M29.[9]