CC/NUMBER 27
JULY 2, 1979

This Week's Citation Classic

Gluck L , Kulovich M V, Borer R C Jr., Brenner P H, Anderson G G & Spellacy W N.
Diagnosis of the respiratory distress syndrome by amniocentesis.
Amer. J. Obstet. Gynecol. **109:**440-45, 1971.
[Depts. Pediat. & Obstet.- Gynecol., Univ. Calif., San Diego Sch. Med., La Jolla, CA]

Amniotic fluid surfactant phospholipids reflect fetal lung development during gestation. Sharply rising lecithin, falling sphingomyelin — ratio of US greater than 2.0 — beyond 35 weeks marks maturity, when delivered newborns are free of respiratory distress syndrome (RDS), or hyaline membrane disease. [The *SCI*® indicates that this paper has been cited over 410 times since 1971.]

Louis Gluck
Department of Pediatrics
University of California
La Jolla, CA 92093

April 3, 1978

"I long had been interested in biochemical development, correlating molecular, morphologic, and physiologic events during growth and maturation of embryos and fetuses. Our model organ, the lung, ideally encompasses all major facets of development. Its unique morphogenesis, easily studied, correlates with its biochemical and physiological maturation. Definable enzymes produce quantifiable surfactant phospholipids in the alveolar lining which lower surface tension and stabilize alveoli, without which life is not possible. There even is a major disease from lack of surfactant in premature humans, hyaline membrane disease (HMD), or respiratory distress syndrome.

"Early in our pioneering studies on biosynthesis of surfactant phospholipids in developing fetal lung my associate Marie V. Kulovich and I found that surfactant is deposited into amniotic fluid. Understanding the developmental biochemistry of lung surfactant allowed these data to fulfill probably the greatest need in management of pregnancy, assessment of fetal lung maturity. Serial amniotic fluids established biochemical maturity of lung at 35-36 weeks gestation in normal pregnancy by matching surfactant phospholipid patterns with clinical maturity. Thus arose lecithin/sphingo myelin or L/S ratios, utilizing these two phospholipid indicators on TLC as a *ratio* to compensate for daily and even hourly variations in amniotic fluid volumes.

"In 1966, we were able to measure maturity of fetal lung by this method. The work began at Yale at a difficult time for obtaining amniotic fluid; only fluids for Rh incompatibility studies during pregnancy were available. A short stay at the University of Miami (academic 1968-69) yielded many samples to verify our findings. In 1969, at the University of California, San Diego, together with Drs. Robert Borer and Roger Freeman we began clinical trials in San Diego and Los Angeles to establish reliability. Thus after three years of laboratory work plus one and a half years of clinical evaluation we felt ready to publish the test for fetal lung maturity, in February 1971. At this time leaders in surfactant studies doubted surfactant was a key factor in hyaline disease, following reports of surplus surfactant in prematures' lungs to stabilize alveoli. The ability to predict fetal lung maturity and thus prevent hyaline membrane disease 'renewed faith' in the central role of surfactant in this disease. The rapid worldwide acceptance of our work has been very gratifying, with daily applicability anywhere babies are delivered, and because it has spurred widespread research into lung development.

"We since have progressed to a more complex, more informative group of measurements, the Lung Profile, including the L/S ratio and percentages of disaturated lecithin, phosphatidyl inositol and phosphatidyl glycerol.[1,2] These last two acidic phospholipids appear necessary to stabilize lecithin in the alveolar layer. The accuracy of prediction of fetal lung maturity by Lung Profile appears as close to 100 percent as a biological test is ever likely to be."

1. Kulovich MV, Hallman MV & Gluck L. The Lung Profile. 1. Normal pregnancy. *Amer J. Obstet. Gynecol.* In press.
2. **Kulovich MV & Gluck L.** The Lung Profile. 2. Complicated pregnancy. *Amer J. Obstet. Gynecol*n press.