NUMBER 2
JANUARY 8, 1979

This Week's Citation Classic

Avery M E & Mead J. Surface properties in relation to atelectasis and hyaline membrane disease. *Am. J. Dis. Child.* **97:** 517-23, 1959.

Low surface tension in the lining of the lung permits stability of the alveoli at end expiration. Lacking such a material, the lung is predisposed to atelectasis. Measurements of the surface tension of lung extracts confirm the presence of a very surface active substance in lungs of infants over 1,000-2,000 gm and in children and adults. In lung extracts of immature infants and infants dying with hyaline membrane disease, surface tension is higher than expected. This deficiency of surface-active material may be significant in the pathogenesis of hyaline membrane disease. [The *SCI*® indicates that this article was cited 376 times in the period 1961-1977.]

Mary Ellen Avery
Department of Pediatrics
Harvard Medical School
Boston, MA 02115

December 29, 1977

"Nearly twenty years have elapsed since we wrote on surface properties in relation to atelectasis and hyaline membrane disease In retrospect, a more fitting title would have been 'Deficient alveolar surfactant in lungs of infants with hyaline membrane disease The word surfactant had not been applied to the alveolar lining layer at that time, indeed the concept of surface tension was not widely appreciated by physicians, most of whom last heard of it in their high school physics course.

"As with most discoveries, the stage was set tor this one by others. Peter Gruenwald, the pathologist, had written on abnormal patterns of expansion in lungs at autopsy and suggested that surface forces might be abnormal. Richard Pattlein England had described the stability of foam of pulmonary edema and wondered if abnormalities would promote atelectasis and transudation Jere Mead at the Harvard School of Public Health had participated with Edward Radford and lames Whittenberger in studies on surface forces in mammalian lungs, and John Clements had demonstrated the essential dependency of surface area and surface tension in lung extracts measured on a Wilhelmv surface balance.

"All that was needed was one person with an interest in lungs of infants, an awareness of the work of physiologists on surface forces, and the encouragement of a preceptor. Jere Mead was the preceptor who actually made the surface balance (out of a paraffin-lined slide box with a strain gauge) on which I carried out the first measurements.

"The results were clear-cut but they only established an association of surfactant deficiency with hyaline membrane disease. Much further work followed, but results came slowly at first. We pursued the morphological aspects; others embarked on biochemical studies. When different approaches gave concordant results, interest in the observation mounted. Only after clinical applicability with the use of the lecithin/sphingomyelin ratio to assess the amount of surfactant in amniotic fluid (shown by Cluck and colleagues) was the essential role of the surfactant widely appreciated and a part of standard textbook teaching.

"It is pleasant not to have to describe the behavior of bubbles on tubes or define surface tension to pediatric audiences in 1979. The message got through.

"Renewed interest in the metabolism of the lung followed, and abnormalities in synthesis and degradation of lung surfactants remain an important area of study. Hyaline membrane disease of the prematurely born infant remains the prototype of diffuse surfactant deficiency. Other causes can occur at other ages, and include fulminant pulmonary edema which washes out surface-active materials, paraquat poisoning, certain viral pneumonias and that group of disorders called adult respiratory distress syndromes. Little wonder that our demonstration of surfactant deficiency in human infants' lungs is widely cited ."