Diagnosis of Surfactant Defects in Newborn, Children and Adults in the Era of Surfactant Therapy*

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Introduction

The risk of the respiratory distress syndrome (RDS) in the newborn is accurately evaluated by studying the lung effluent phospholipids (Cosmi 1987; Hallman 1984; Hallman et al. 1986a). In adult respiratory distress syndrome (ARDS) there is also a severe defect among the bronchoalveolar lavage phospholipids (Hallman et al. 1982). Surfactant defects appear early in respiratory failure, and the surface activity of the lung effluent deteriorates concurrent with the appearance of respiratory failure and correction of the surfactant defect ameliorates the respiratory failure (Lachmann et al. 1987). Although the surfactant system appears to be of central importance in the pathogenesis of respiratory failure, there are inherent limitations in obtaining the lung effluent and to study surfactant function and metabolism in situ. It has been claimed that the airway specimen, recovered during partial lung lavage, may not be representative of alveolar fluid. Secondly, there may be no reliable methods to quantify the surfactant pool. In this report it is proposed that surfactant diagnostics are of value when surfactant therapy is contemplated.

Methodology

Recovery of Lung Effluent

Lung effluent may be obtained during routine suctioning of the airways. In most cases the catheter is not wedged, but instead advanced to the main bronchus, and a small quantity of saline (0.5–10 ml depending on the size of the patient) is introduced. Shortly thereafter, the central airways are suctioned, and the small volume airway specimen is collected into a trap.

For bronchoalveolar lavage (BAL) a bronchoscope or a catheter is wedged to a lung segment. Thereafter, five to sixty milliliters of normal saline is injected to lung periphery. Fluid from the airways is then suctioned through the

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bronchoscope and collected to a container. The procedure may be repeated. This technique is similar to the quantitative BAL that involves lavage of the whole lung through the trachea.

**Measurement of Surfactant and Its Activity**

There are several possibilities for surfactant analysis in lung effluent. In the following brief discussion we point out the various approaches. Some of them may not be accurate. *Post mortem* analysis of surfactant is not discussed here.

*Concentration or Amount of Surfactant Components.* In emphysema the concentration and the recovery tend to decrease, possibly reflecting a decrease in lavageable alveolar area but not necessarily a deterioration in the surfactant system. We believe that measurements of the concentration or the amount of surfactant are not suitable for accurate diagnosis of the surfactant status (Hallman et al. 1982).

*Concentration in Alveolar Epithelial Lining Fluid.* The concentration of surfactant components in alveolar epithelial lining fluid may be estimated using an internal standard that readily crosses cellular membranes and therefore has an uniform concentration in extracellular fluids. The volume of epithelial lining fluid is obtained on the basis of the Fick principle by comparing concentration of urea in BAL fluid to that in serum. However, some urea diffuses into BAL fluid during multiple lavage, leading to an overestimate of the volume and underestimate of the concentration of surfactant component (Marcy et al. 1987).

*Reference Compounds.* The expression of surfactant component or surface activity on the basis of the reference compound is currently the method of choice for diagnostic purposes (Hallman 1984). The possible references include sphingomyelin, total phospholipid, albumin or total protein. The frequently used indexes include the saturated phosphatidylcholine/sphingomyelin ratio (the L/S ratio), phosphatidylglycerol/total phospholipid (PG), and minimum surface activity adjusted to a constant phospholipid concentration.

*Fractionation of Lung Effluent.* The acellular sample may be processed according to techniques used for subcellular fractionation. The phospholipids may be separated from the protein-rich fraction by centrifugation. The density gradient centrifugation allows the isolation of the membranous fraction, enriched with the surface active complex (Kankaanpää and Hallman 1982; Hallman et al. 1982).

*External markers.* Specific markers, attached to exogenous surfactant, may be used to study both the turnover of the complex and to estimate the surfactant pool size (Hallman et al. 1986b).