

# A Biochemical View of Lung Surfactant and RDS

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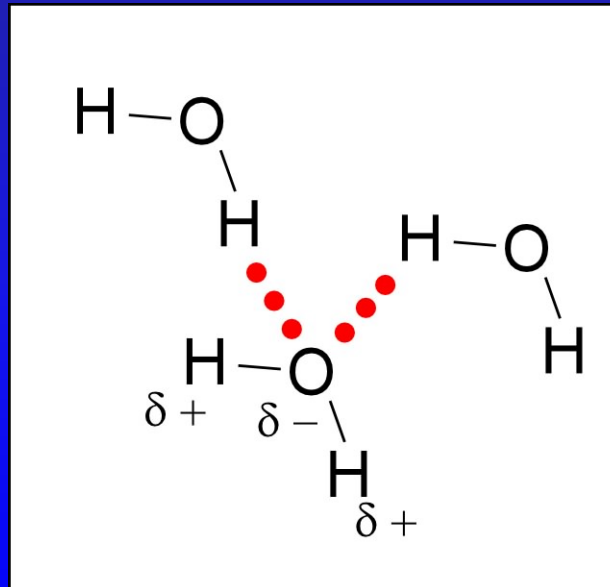
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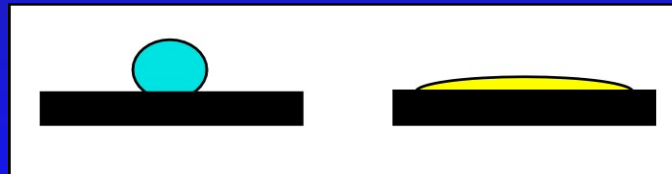
# Properties of Water

- ❖ Very Polar
- ❖ High boiling point
- ❖ Forms large network of hydrogen bonds



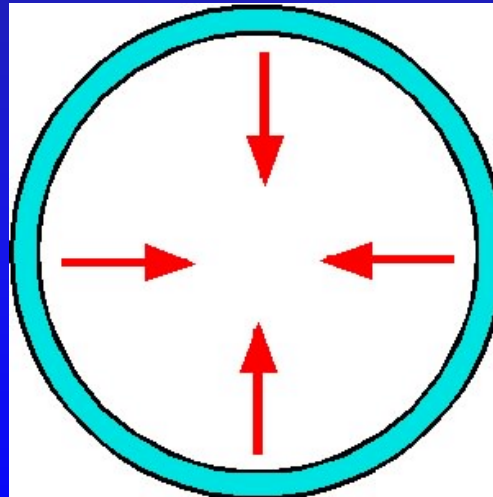
# Surface Tension

- ❖ Water has a **VERY HIGH** surface tension
- ❖ Water will attempt to **minimize** its surface area in contact with air



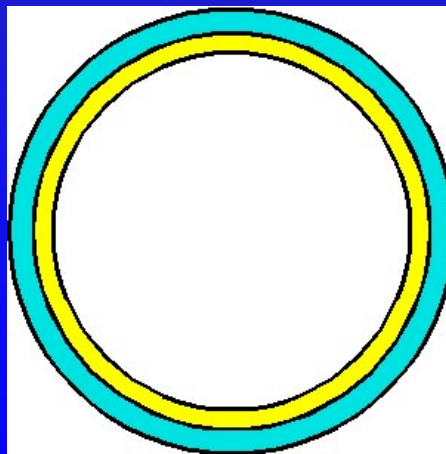
# Surface Tension

- ❖ An air-filled sphere coated with water has a tendency to collapse (reach a minimum volume) due to the pulling force of water surface tension



# Lung Surfactant

- ❖ Alveoli are coated with **lung surfactant** in order to reduce the surface tension of water, thus preventing collapse (atelectasis) upon exhalation and decreasing the force necessary to expand the alveoli upon inhalation





# Production of Surfactant

- ❖ Produced in **Type II** alveolar epithelial cells
- ❖ Exported as **lamellar bodies** to the alveolar surface
- ❖ Contains a mixtures of lipids and proteins



# Composition of Surfactant

## ❖ Major Lipids (~90%)

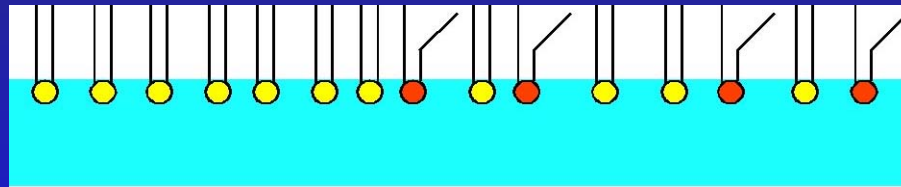
- ▶ Saturated Phosphatidylcholine  
**DPPC** (Lecithin) 60-80%
- ▶ Unsaturated Phosphospholipids  
Phosphatidylglycerol (**PG**) ~10%

## ❖ Major Proteins (~10%)

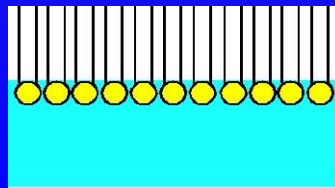
- ▶ Hydrophilic (**SP-A** & **SP-D**)
- ▶ Hydrophobic (**SP-B** & **SP-C**)

# Function of Surfactant

- ❖ Lipids form a monolayer at the air-water interface



- ❖ Surface tension decreases as lipid monolayer is compressed







# Role of Lipid Components

## ❖ DPPC

- ▶ Forms stable condensed monolayers
- ▶ Poor at spreading

## ❖ PG (and other unsaturated lipids)

- ▶ Interacts with proteins
- ▶ Helps DPPC to spread



# Role of Protein Components

- ❖ **Hydrophilic (SP-A and SP-D)**
  - ▶ Immune functions
  - ▶ Transport to alveolar surface
- ❖ **Hydrophobic (SP-B and SP-C)**
  - ▶ Monolayer adsorption and fluidity
  - ▶ Other properties?



# SP-A

- ❖ Glycoprotein (collectin)
- ❖ Binds phospholipids – role in tubular myelin
- ❖ SP-A knock-out mice survive
- ❖ May help to regulate surfactant production by type II cells



# SP-D

- ❖ Glycoprotein (collectin)
- ❖ Poor binding to phospholipids
- ❖ Enhance phagocytosis of bacteria?
- ❖ Helps to clear inhaled pollutants without inflammation



# SP-B

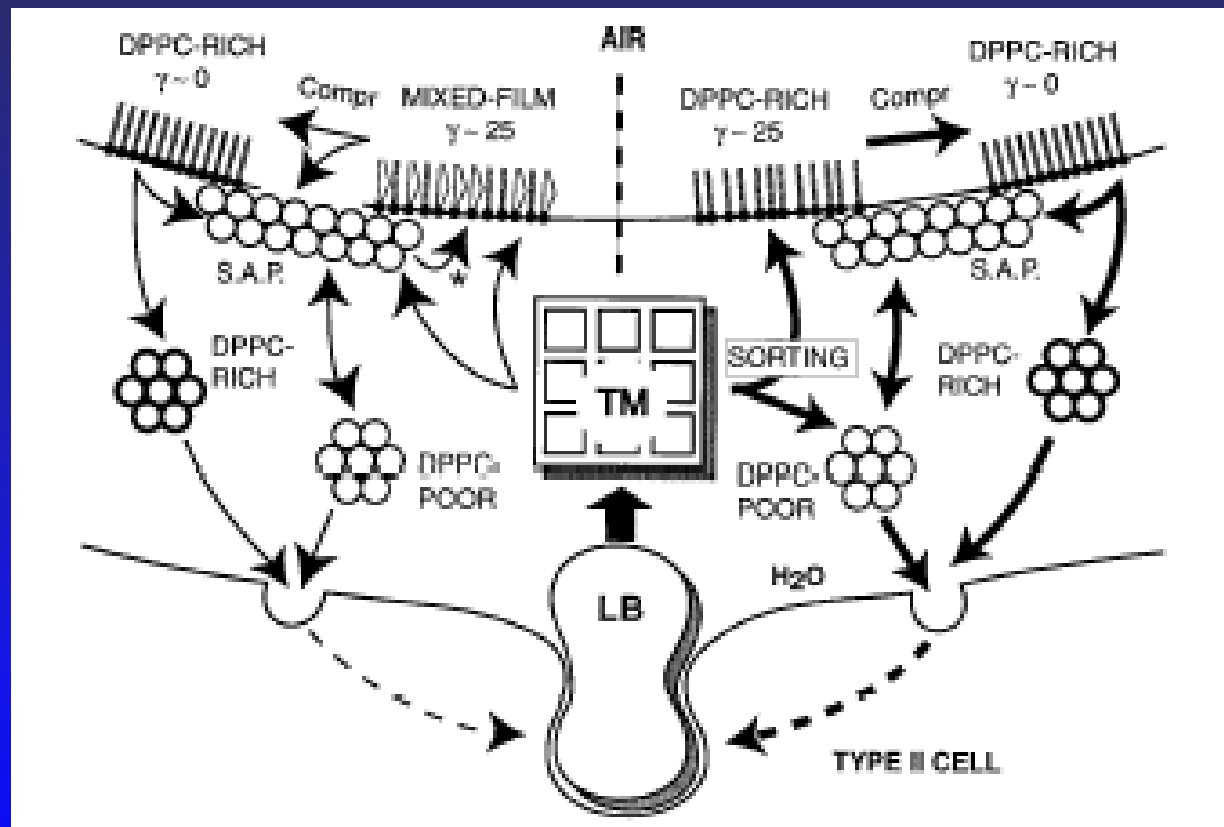
- ❖ Absolutely required for survival
- ❖ Tubular myelin component
- ❖ Enhances adsorption and resreading
- ❖ Fluidizes monolayer and helps to prevent collapse



# SP-C

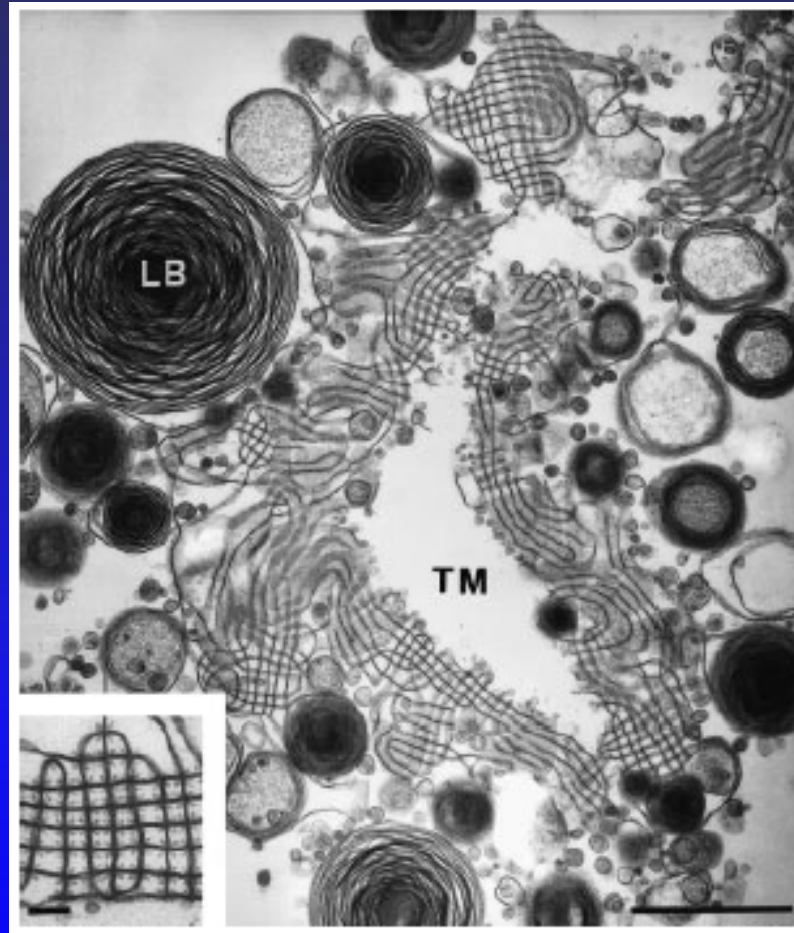
- ❖ Smallest and most hydrophobic protein
- ❖ Contains 2 fatty acid chains
- ❖ Increases rate of adsorption
- ❖ SP-C null mice survive but have breathing problems

# Cartoon of Surfactant Cycling



From J. Goerke, Pulmonary surfactant: functions and molecular composition  
Biochim. Biophys. Acta 1408 (1998) 79-89

# EM of Lamellar Bodies and Tubular Myelin



From J. Goerke, Pulmonary surfactant: functions and molecular composition  
*Biochim. Biophys. Acta* 1408 (1998) 79-89





# Respiratory Distress Syndrome

- ❖ RDS is a serious clinical problem
  - ▶ Most common cause of neonatal mortality
  - ▶ High incidence in premature births
- ❖ Caused by insufficient lung surfactant
- ❖ Requires supportive care
  - ▶ Oxygenation
  - ▶ Ventilation
- ❖ May require surfactant replacement therapy (SRT)



# Testing for Lung Maturity

- ❖ L/S ratio
  - ▶ Separates lecithin (PC) and sphingomyelin from amniotic fluid by TLC
  - ▶  $L/S > 2$  indicates mature lung
- ❖ PG assay by latex agglutination
- ❖ Fluorescence polarization of amniotic lipids
- ❖ Foam stability index
- ❖ Lamellar body count



# Surfactant Replacement Therapy

- ❖ Natural Surfactant

- ▶ Survanta (beractant) – Abbott Labs
- ▶ Modified bovine lung extract

- ❖ Synthetic Surfactant

- ▶ Exosurf Neonatal – GlaxoSmithKline
- ▶ Protein-free
- ▶ Contains DPPC, cetyl alcohol and a synthetic polymer

- ❖ New Developments

- ▶ Synthetic versions of SP-B and SP-C

- ❖ See AAP Policy Statement on SRT



# Surfactant Replacement Therapy for Respiratory Distress Syndrome (RE9829)

## AMERICAN ACADEMY OF PEDIATRICS

Committee on Fetus and Newborn

**ABSTRACT.** Respiratory failure secondary to surfactant deficiency is a major cause of morbidity and mortality in low birth weight immature infants. Surfactant therapy substantially reduces mortality and respiratory morbidity for this population. The statement summarizes the indications for surfactant replacement therapy. Because respiratory insufficiency may be a component of multiorgan dysfunction in sick infants, surfactant should be administered only at institutions with qualified personnel and facilities for the comprehensive care of sick infants.

Exogenous surfactant replacement has been established as an appropriate preventive and treatment therapy for prematurity-related surfactant deficiency. Surfactant therapy also may be indicated for more mature infants with primary pulmonary hypertension or meconium aspiration syndrome. Single and multicenter randomized controlled trials using synthetic, modified animal, purified animal, and human surfactants have shown that the use of surfactant replacement in preventive or treatment modes has been safe and efficacious.<sup>1-18</sup> Reduced mortality rates and improved short-term respiratory status for preterm infants with surfactant-deficiency respiratory distress have been confirmed. However, coexistent morbidity, such as necrotizing enterocolitis, nosocomial infections, patent ductus arteriosus, intraventricular hemorrhage, and chronic lung disease, appear primarily unaffected. Reports of long-term outcome for infants enrolled in the randomized surfactant trials and evaluated at 1 to 2 years of age have shown neither beneficial nor adverse effects of surfactant use on growth and/or neurodevelopmental parameters.<sup>19-26</sup>

Current studies continue to address refinements in surfactant use that may optimize its effectiveness. New products, timing, dosage, methods of administration, and modification for particular gestational age groups are among the issues that may improve the effect of surfactants. Two surfactants, one synthetic and the other modified bovine, have been licensed and are available commercially in the United States.

Universal availability of these products raises the concern that surfactants may be used to address the respiratory component of multisystem disorders that affect high-risk, low birth weight infants when other diseases cannot be addressed appropriately. This is a critical issue because the target population for surfactant therapy is primarily the high-risk, low birth weight infants who may have multisystem disorders that are not affected beneficially by treatment with surfactants. Caring for these infants in nurseries without the full range of capabilities required may affect the overall outcome adversely.<sup>27,28</sup> As systems of neonatal health care adapt to modified patterns of disease in low birth weight infants, the following recommendations should be incorporated.

## RECOMMENDATIONS

1. Surfactant replacement therapy should be directed by physicians qualified and trained in its use and administration. Qualifications should include experience in management of the respiratory care of low birth weight infants, particularly those on mechanical ventilation.
2. Nursing and respiratory therapy personnel experienced in the management of low birth weight infants, including mechanical ventilation, should be available within the unit at the bedside when surfactant therapy is administered.
3. Equipment necessary for managing and monitoring the condition of low birth weight infants, including that needed for mechanical ventilation, should be available on-site when surfactant therapy is

administered. Radiology and laboratory support to manage a broad range of needs of these infants should be available.

4. More important, surfactant therapy should be used only in institutions in which facilities and personnel are available for the management of multisystem disorders and low birth weight infants.
5. An institutionally approved surfactant therapy protocol, which is a mandatory component of the quality assurance program for neonates, should exist.
6. In the institutions not satisfying recommendations 2 through 5, and when timely transfer to an appropriate institution cannot be achieved, surfactant therapy may be given, but only by a physician skilled in endotracheal intubation. Under these circumstances, consultation with a subspecialty center should be obtained. Infants should be transferred from such institutions if appropriate and when feasible to a center with appropriate facilities and staff trained to care for multisystem morbidity in low birth weight infants.

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The recommendations in this statement do not indicate an exclusive course of treatment or serve as a standard of medical care. Variations, taking into account individual circumstances, may be appropriate.

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