Pulmonary Surfactant

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Pediatric PGY-2

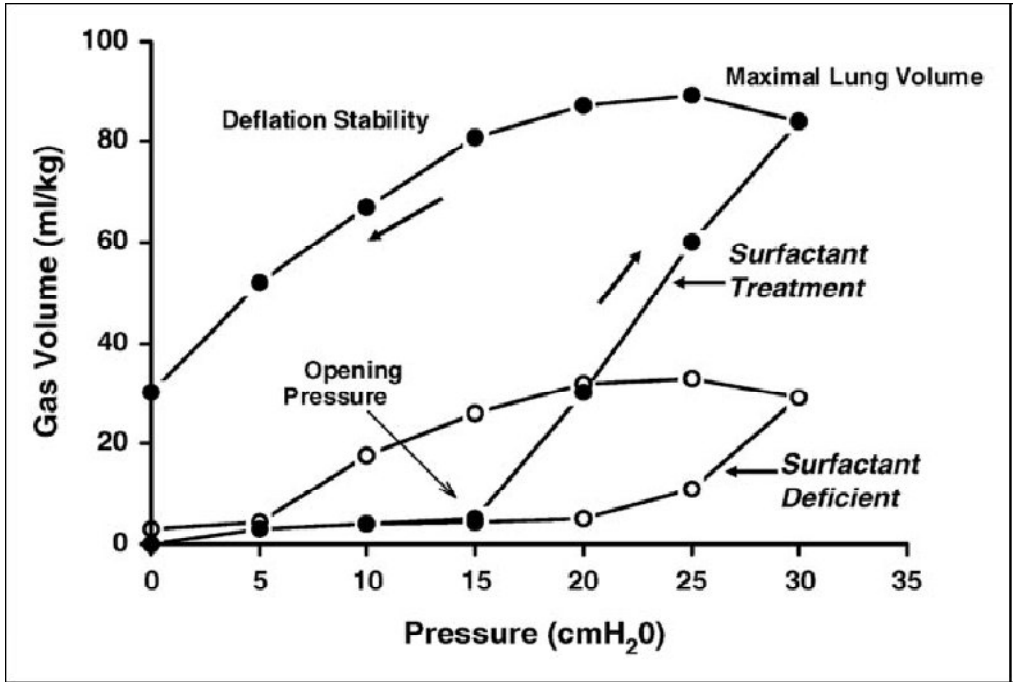
Objectives

- Functions
- Composition
- Metabolism
- Applications

Functions

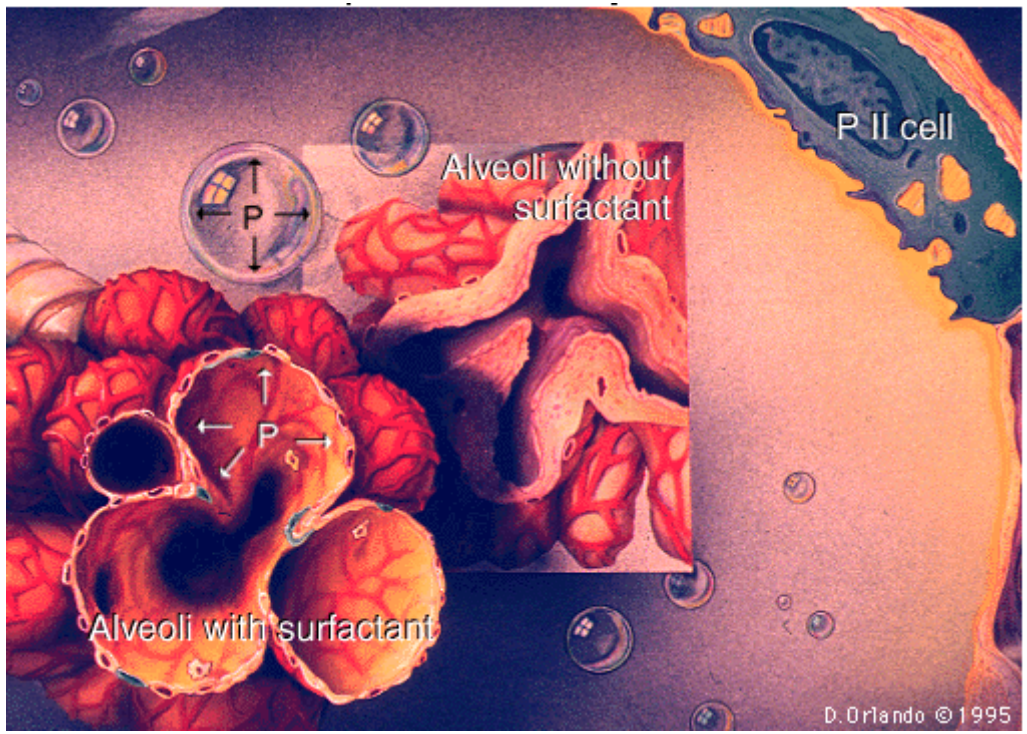
- To increase pulmonary compliance
- To prevent the lung from collapsing at the end of expiration
- To keep alveoli dry
- To regulate the size of alveoli
- To play roles in pulmonary host defense

Pulmonary Compliance



Pressure-volume curves for a surfactant-deficient preterm lung and a surfactant-treated lung. Surfactant facilitates inflation of the lung from a lower pressure, permits the lung to open to a higher volume, and prevents the lung from collapsing when pressure is decreased (deflation stability).

Pulmonary Compliance



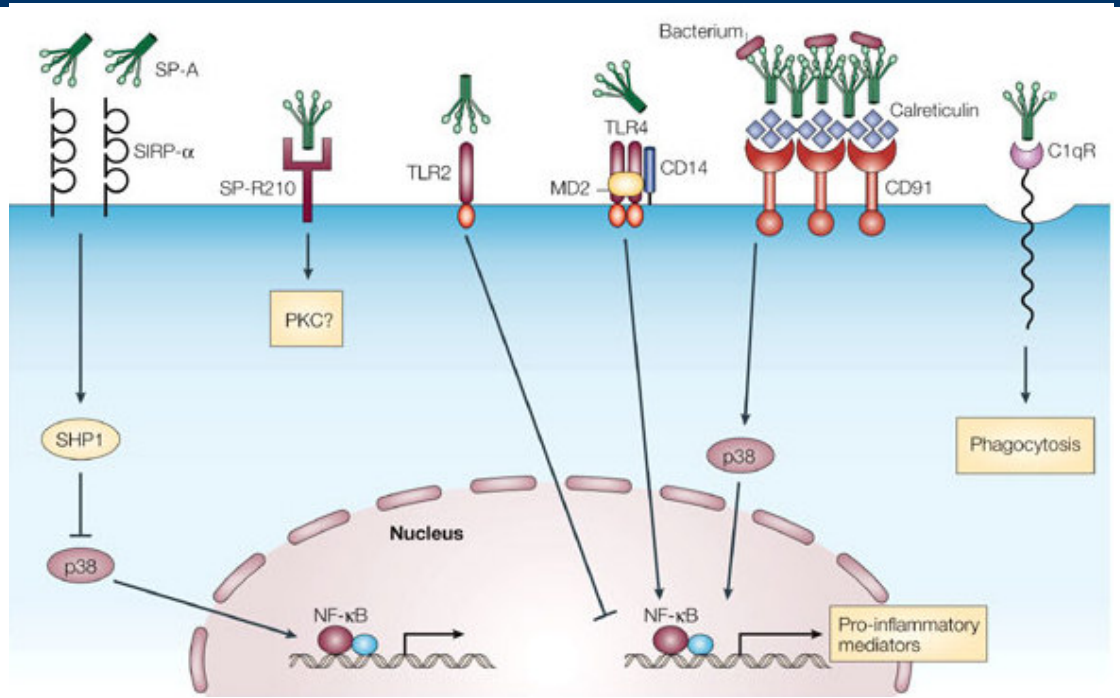
Pulmonary Surface Tension

- Pulmonary surfactant greatly reduces surface tension,
  - The normal for water is 70 dyn/cm (70 nN/m), for the lungs is 25 dyn/cm (25 mN/m)
  - At the end of the expiration, compressed surfactant phospholipid molecules decrease the surface tension to very low, near-zero levels

Pulmonary Surface Tension

- Keep the alveoli dry
  - The reduction in surface tension reduces fluid accumulation in the alveolus as the surface tension draws fluid across the alveolar wall.
- Regulate the alveolar size
  - The increase in surface tension (as the alveoli increase in size, the surfactant becomes more spread out over the surface of the liquid):
    - Slows the rate of increase of the alveoli.
    - Helps all alveoli expand at the same rate (as one that increases more quickly will experience a large rise in surface tension slowing its rate of expansion).
    - Regulates the rate of shrinking(as if one reduces in size more quickly the surface tension will reduce more so other alveoli can contract more easily than it).

Host Defense

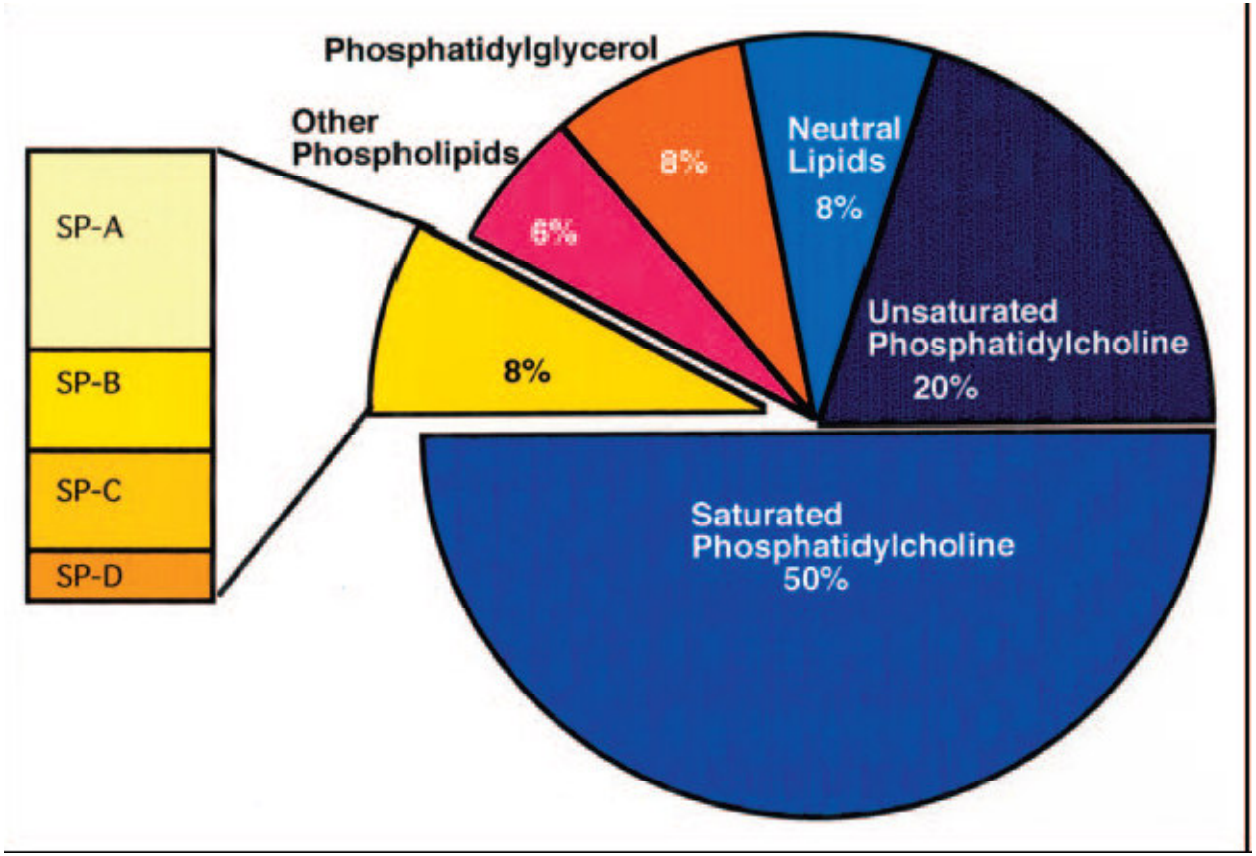


SP-Aand D Confer innate immunity (carbohydrate recognition domains allowing them to coat bacteria and viruses promoting phagocytosis by macrophages

Composition

- **Lipids**
  - Over 90% of the surfactant
  - 50% dipalmitoylphosphatidylcholine (DPPC).
    - A phospholipid with two 16-carbon saturated chains and a phosphate group with quaternary amine group attached.
    - Phosphatidylcholine: ~85% of the lipid in surfactant with saturated acyl chains.
    - Phosphatidylglycerol (PG): 11% of the lipids in surfactant with unsaturated fatty acid chains that fluidize the lipid monolayer at the interface.
    - Neutral lipids and cholesterol are also present.

Composition



Composition

- **Proteins**
  - 10% of surfactant.
  - Apoproteins SP-A , B , C and D.

Composition

- **Surfactant protein A and D**
  - Confers innate immunity
  - Involved in a negative feedback mechanism to control the production of surfactant.

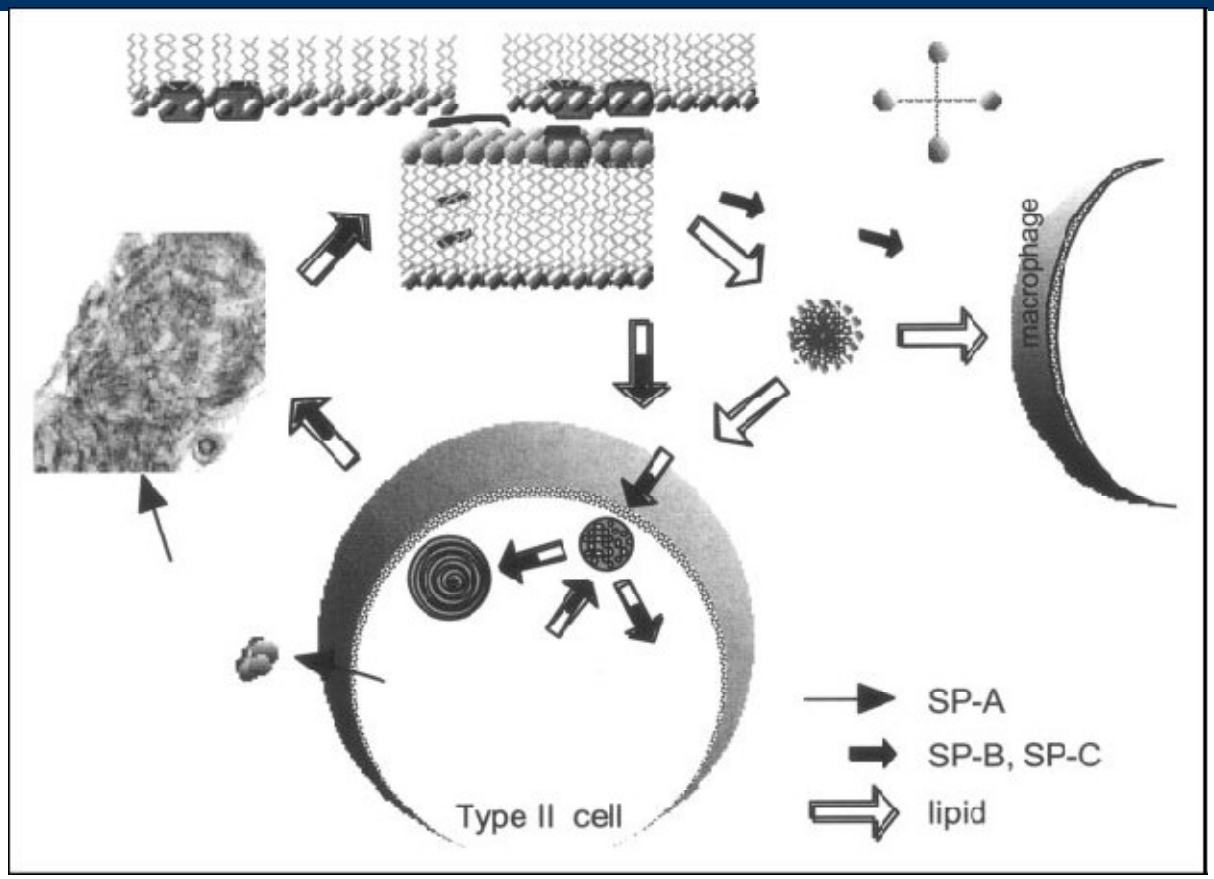
Composition

- **SP-B and SP-C**
  - Hydrophobic membrane proteins that increase the rate that surfactant spreads over the surface.
  - Required for proper biophysical function of the lung.
    - Humans and animals born with a congenital absence of SP-B suffer from intractable respiratory failure
    - Those born lacking SP-C tend to develop progressive interstitial pneumonitis

Surfactant metabolism

- Synthesized mainly by type II alveolar epithelial cells, also by airway epithelial and Clara cells.
- Stored as closely packed bilayers in lamellar bodies, which serve as the intracellular storage of surfactant.
- Secreted into the alveoli by exocytosis

Surfactant metabolism



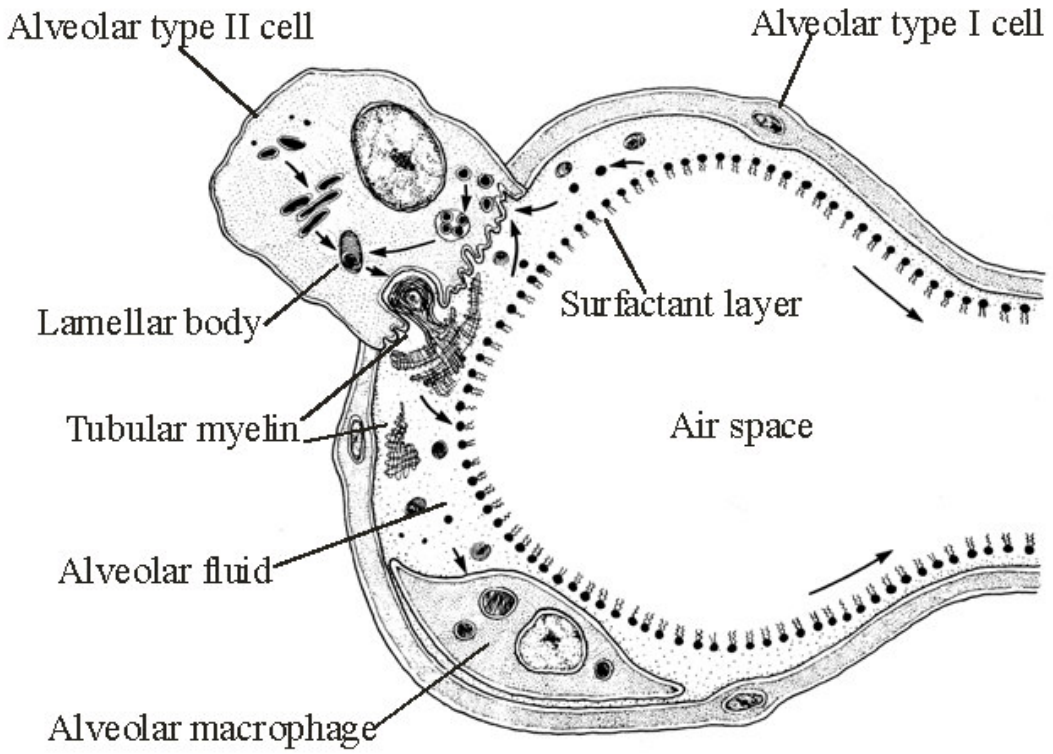
Surfactant metabolism

- The lamellar body phospholipids rearrange in the alveoli into an expanded membrane lattice called tubular myelin which is at the air-fluid interface just above the alveolar epithelium.
- The hydrophobic SP-B, C, are secreted in the lamellar bodies together with phospholipids.
- The hydrophilic SP-A,D are secreted independently of lamellar bodies, and associate with surfactant lipids in the alveolar lumen.

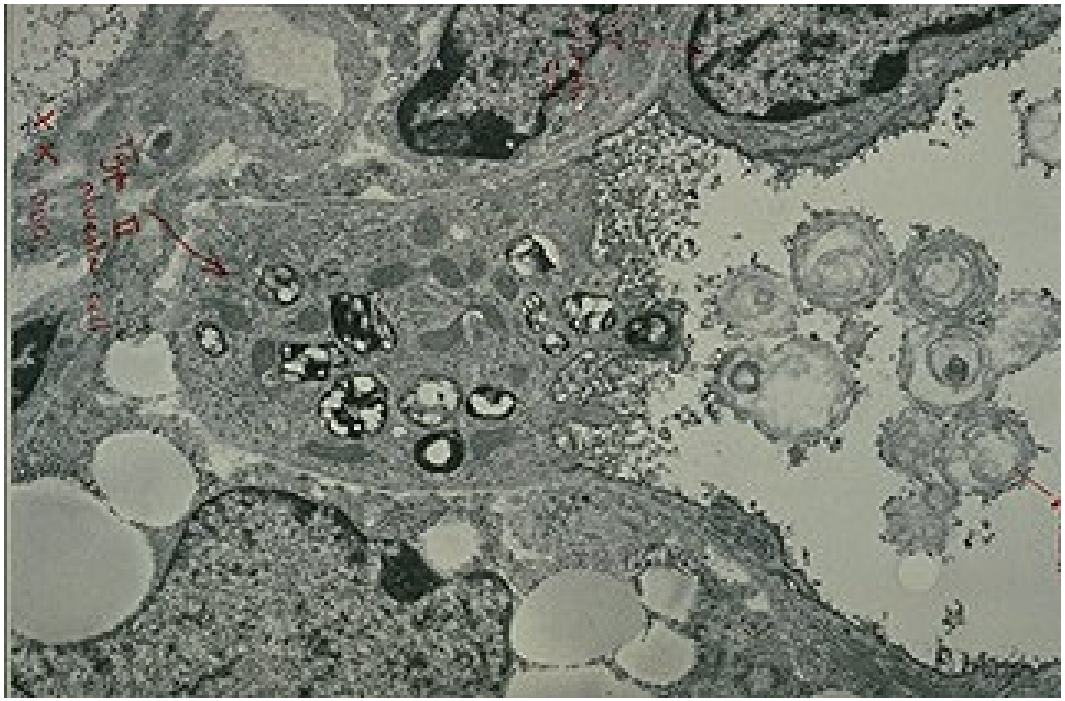
Surfactant metabolism

- Recycled into type II cells and re-utilized or removed from the cycle by phagocytosis and degraded in alveolar macrophages

Surfactant metabolism



Surfactant metabolism



Surfactant metabolism

- Lamellar bodies appear in the cytoplasm at about 20 weeks gestation.
- Term infants are estimated to have an alveolar storage pool of approximately 100mg/kg of surfactant, while preterm infants have an estimated 4-5mg/kg at birth. .
- Up to 90% of surfactant phosphatidylcholine is recycled from the alveolar space in the newborn.

Applications

Diseases

- RDS in premature babies <28-32 weeks of gestation. HMD is pathological Dx.
- Congenital surfactant deficiency
- Pulmonary alveolar proteinosis

Applications

Variables That Contribute to Distribution

- Surface Activity Essential for rapid adsorption and spreading
- Surfactant distributed with fluid by gravity in large airways
- The higher the volume, the better the distribution
- Rapid administration results in a better distribution
- Pressure and positive end-expiratory pressure clear airways of fluid
- Higher volumes of fetal lung fluid or edema fluid may result in a better distribution

Applications

Synthetic pulmonary surfactants

- Exosurf - a mixture of DPPC with hexadeconal and tyloxapol added as spreading agents
- Pumactant (Artificial Lung Expanding Compound or ALEC) - a mixture of DPPC and PG
- KL-4 - composed of DPPC, palmitoyl-oleoyl phosphatidylglycerol, and palmitic acid, combined with a 21 amino acid synthetic peptide that mimics the structural characteristics of SP-B.
- Venticute - DPPC, PG, palmitic acid and recombinant SP-C

Applications

Animal derived surfactants

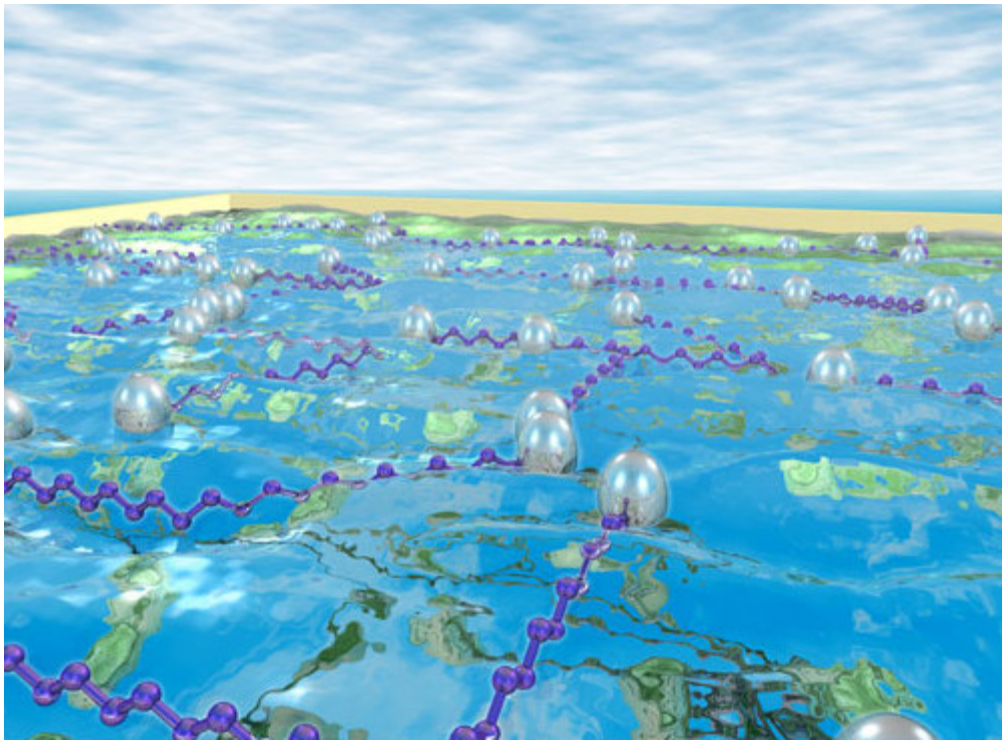
- Alveofact - from cow lung lavage fluid
- Curosurf - from material derived from minced pig lung
- Infasurf - from calf lung lavage fluid
- Survanta - from minced cow lung with additional DPPC, palmitic acid and tripalmitin

Exosurf, Curosurf, Infasurf, and Survanta are the surfactants currently FDA approved for use in the U.S.

Reference

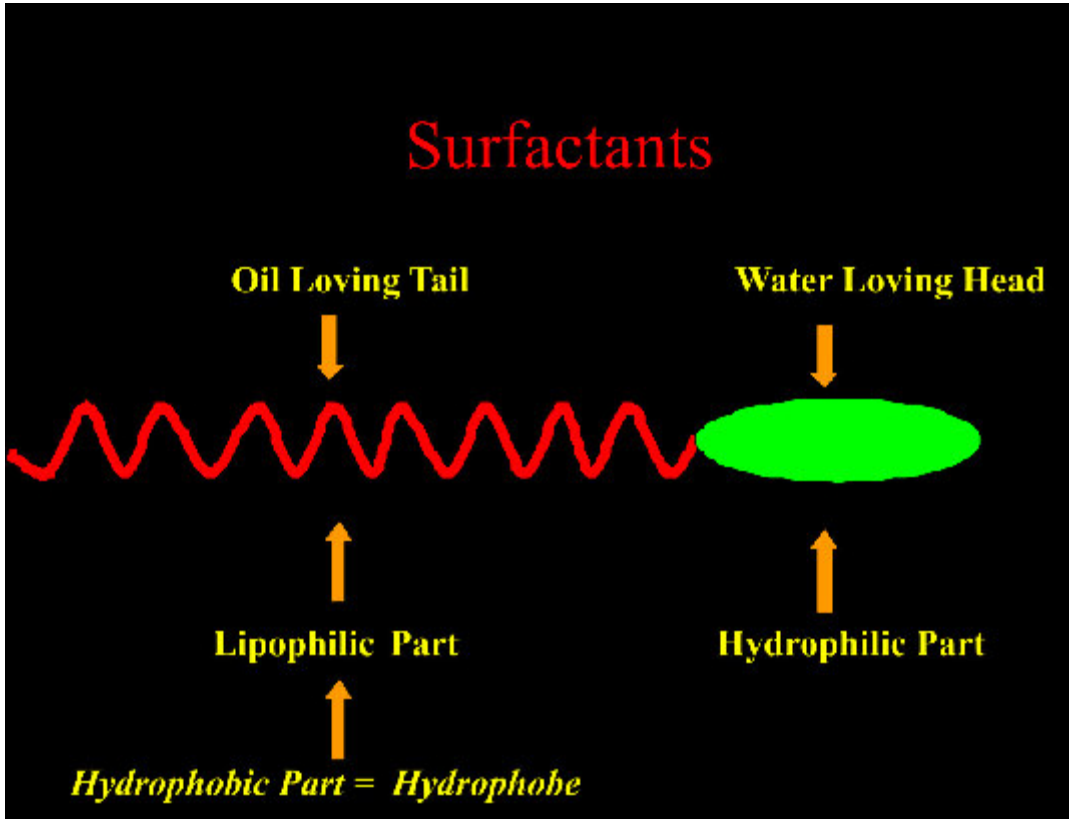
- ***Why Surfactant Works for Respiratory Distress Syndrome*** *Alan H. Jobe, MD, PhD* **NeoReviews** Vol.7 No.2 February 2006 e95*
- ***Historical Perspectives: Neonatology: The Long View*** *A. G.S. Philip and R. Usher NeoReviews, January 1, 2005; 6(1): e3 - e11.*
- ***Prevention of respiratory distress syndrome in preterm infants Author*** *Stephen E Welty, MD uptodate 2009*
- ***Exogenous surfactant therapy in preterm infants Author*** *Stephen E Welty, MD uptodate 2009*

Thank you!



Pulmonary Compliance

- **Hysteresis**
  Volume change per unit of pressure change across the lung. Measurements of lung volume obtained during the controlled inflation/deflation of a normal lung show that the volumes obtained during deflation exceed those during inflation, at a given pressure. This difference in inflation and deflation volumes at a given pressure is called hysteresis which due to the presence of surfactant.


Surfactants
Oil Loving Tail
Water Loving Head
Lipophilic Part
Hydrophilic Part
Hydrophobic Part = Hydrophobe