Pulmonary Surfactant

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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).

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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-A and D confer innate immunity (carbohydrate recognition domains allowing them to coat bacteria and viruses promoting phagocytosis by macrophages

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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

- Saturated Phosphatidylcholine (50%)
- Unsaturated Phosphatidylcholine (20%)
- Neutral Lipids (8%)
- Other Phospholipids (6%)
- Phosphatidylglycerol (8%)

Compounds:
- SP-A
- SP-B
- SP-C
- SP-D
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 hexa-deconal 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**

- **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!
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.