

PBL

☐ Sheet

☒ Slide -*Edited*

☐ Handout

Number

2

Subject

Clinical Overview

Done By

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Date: 25/12/2016

Price:

Respiratory distress syndrome



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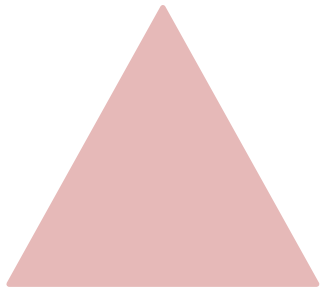
Third year medical
students

12 / December/2016

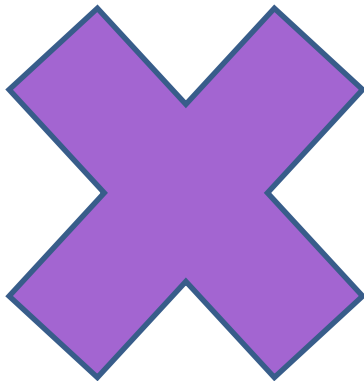
Priority levels



Important!



Read it quickly



Not Important

Outlines

- **Definition**
- **Physiology**
 - Respiration
 - Surface tension
 - Lung compliance
 - Lung volume
 - surfactant
- **Respiratory distress syndrome**
 - Pathophysiology
 - Incidence
 - Presentation
 - management



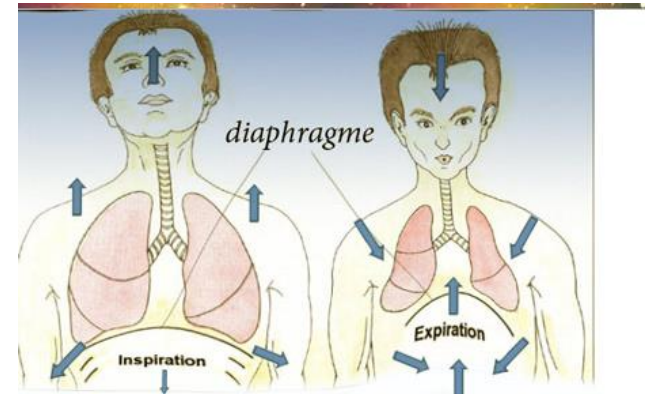
Respiration = the series of **exchanges** that leads to the uptake of oxygen by the cells, and the release of carbon dioxide to the lungs



Step 1 = ventilation
– **Inspiration & expiration**



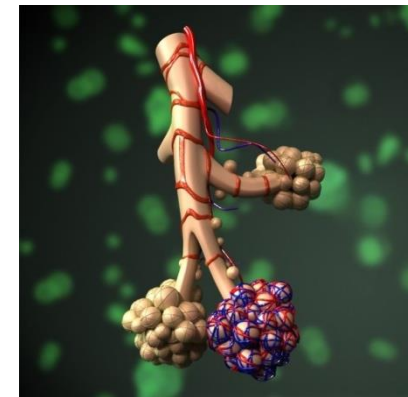
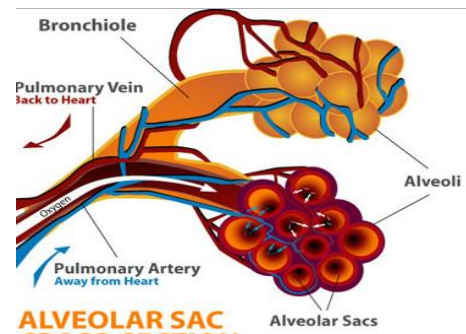
Step 2 = **exchange between alveoli** (lungs) and pulmonary capillaries (blood)
– Referred to as *External Respiration*



Step 3 = **transport of gases** in blood



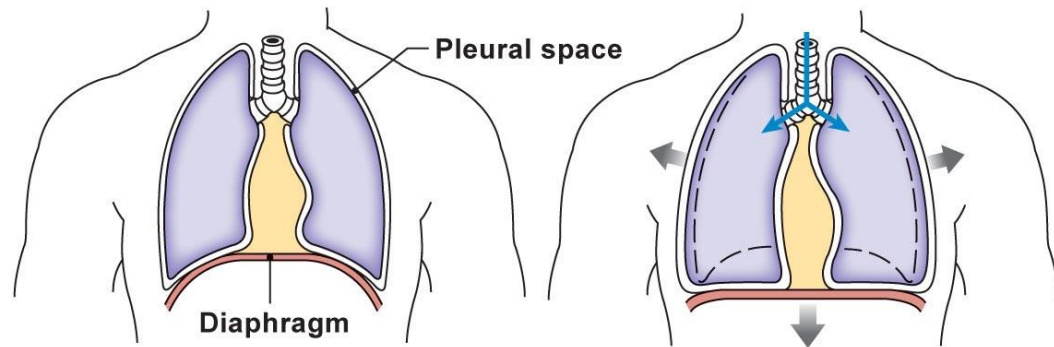
Step 4 = **exchange between blood and cells**
– Referred to as *Internal Respiration*



Ventilation = (inspiration + expiration) responsible muscles

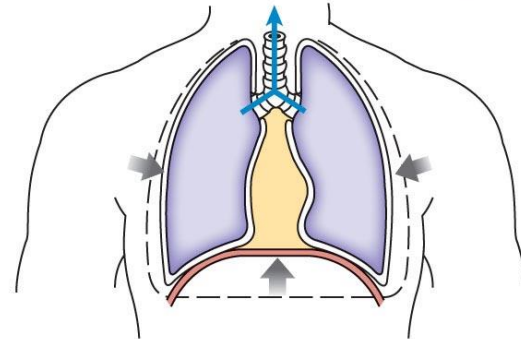
➤ The diaphragm (only creates about 60-75% of the volume change during inspiration)

➤ The muscles of **inspiration** (external intercostals muscles) & muscles of expiration (internal intercostals muscles)



(a) At rest, diaphragm is relaxed.

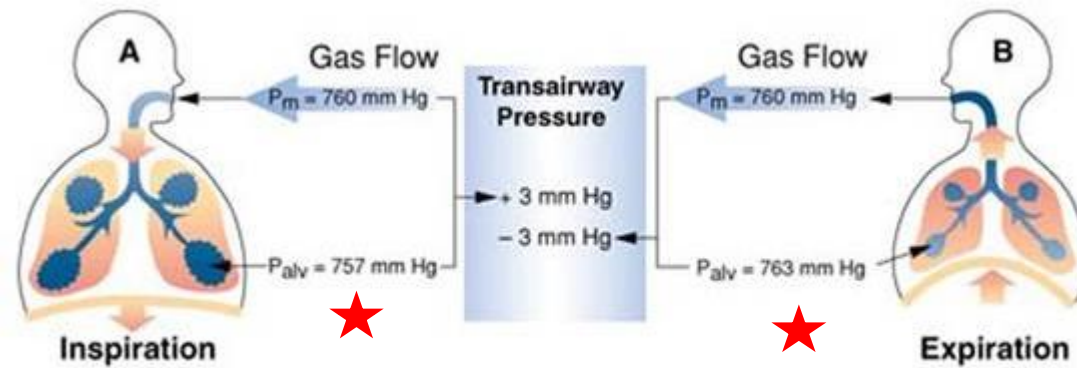
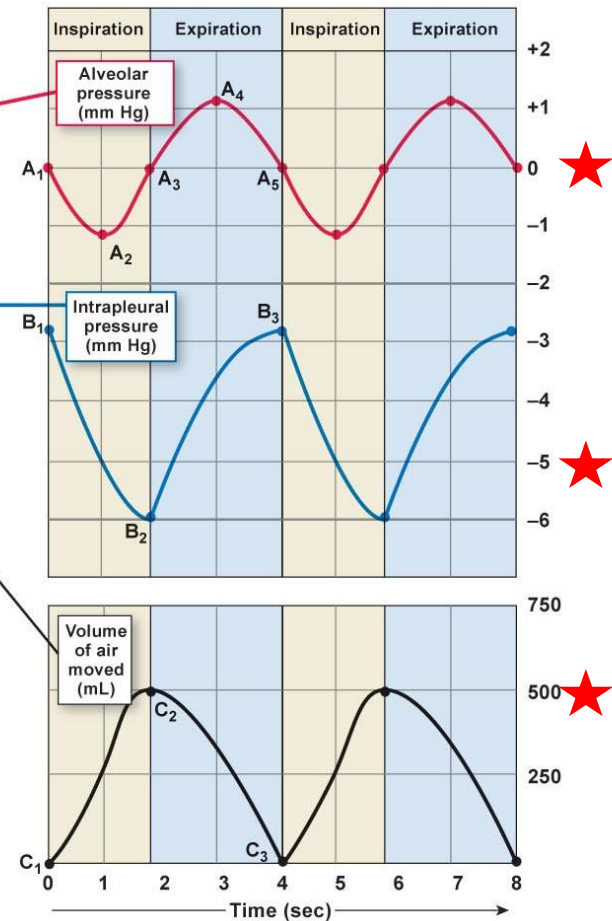
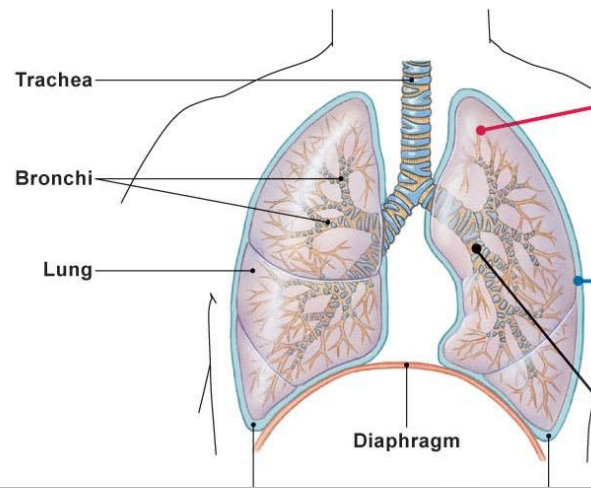
(b) Diaphragm contracts, thoracic volume increases.



(c) Diaphragm relaxes, thoracic volume decreases.

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Ventilation



Tidal volume in new born = 4 – 6ml / kg

If baby weigh=3kg

TV = 12 - 18 ml



Minute ventilation

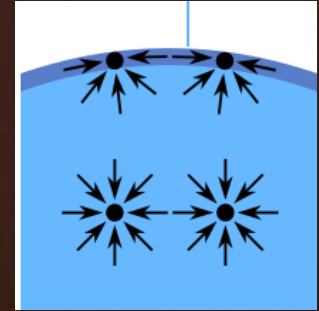
$$\text{Minute volume} = \text{Tidal Volume} \times \text{Frequency}$$

$$\begin{aligned}\text{Minute ventilation} &= \text{Tidal volume} \times \text{RR} \\ &= 500 \text{ ml/b} \times 20 \text{ b/min} = 10000 \text{ ml/min}\end{aligned}$$

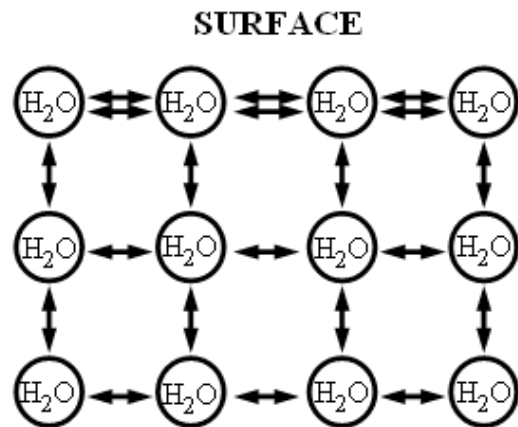
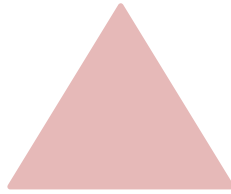
But if for some reason tidal volume decreased to let's say 250ml, RR should increase to 40 to compensate, so:

$$250 \times 40 = 10000 \text{ ml/min} \rightarrow \text{Tachypnea}$$

Surface tension

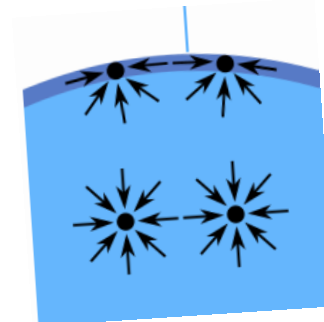


An air-filled sphere coated with water has a tendency to collapse (reach a minimum volume) due to the pulling force of water surface tension



Stronger

Surface tension—molecules at the surface form stronger bonds

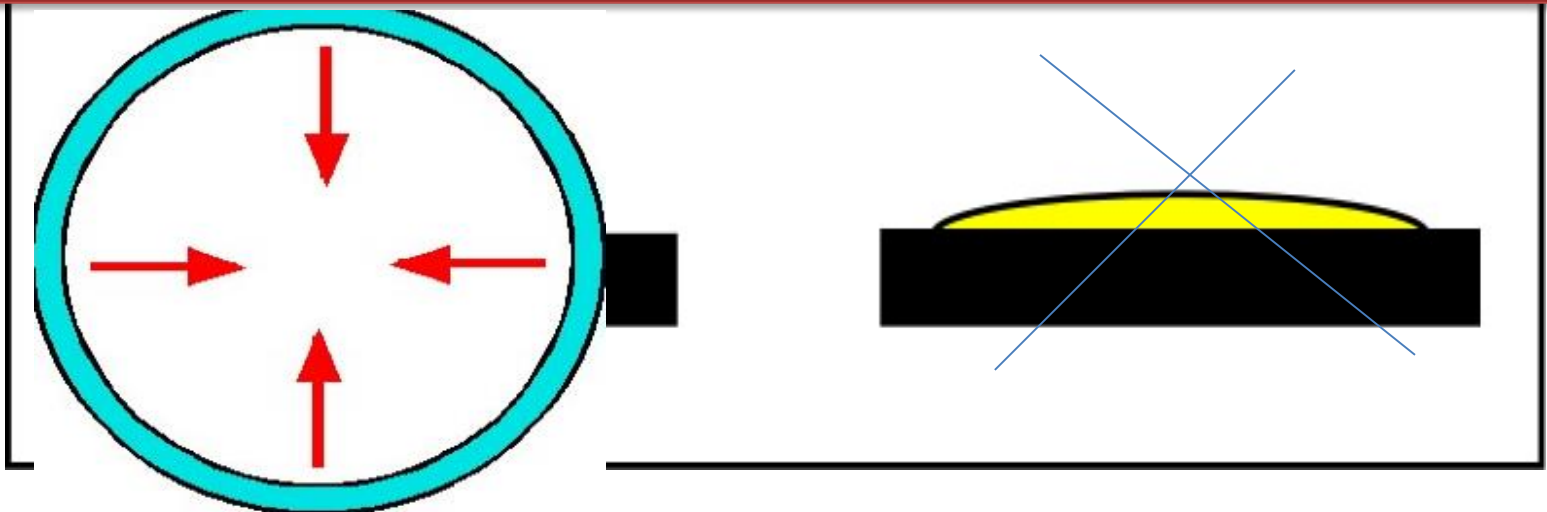


Surface Tension

Water has a VERY HIGH surface tension

Water will attempt to minimize its surface area in contact with air

Surface tension : Attractive forces between molecule at air water interface

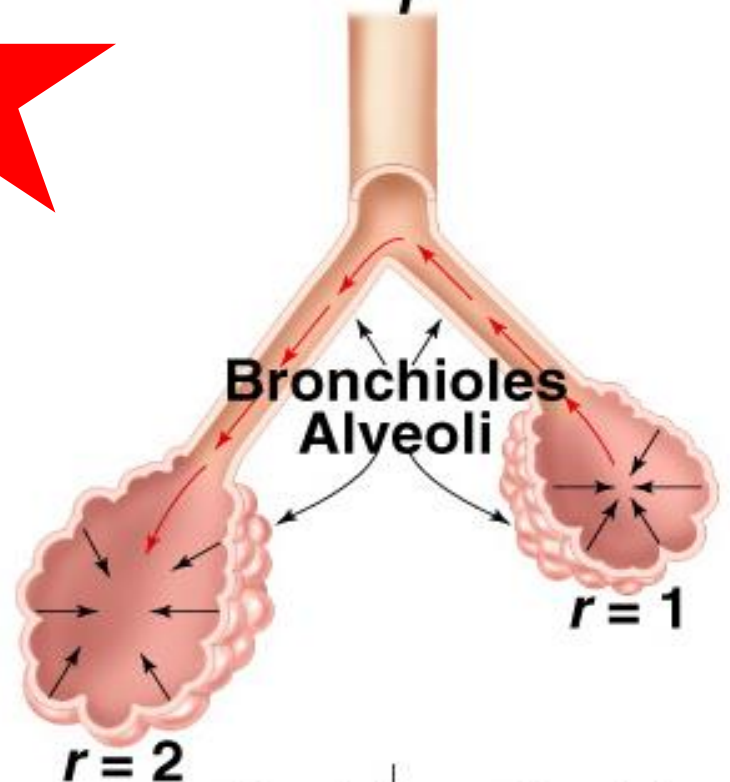


Law of Laplace

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Law of Laplace

$$P = \frac{2 \times T}{r}$$



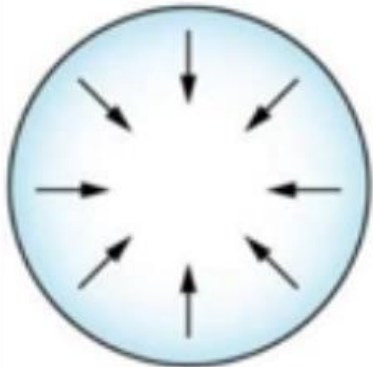
$$\begin{array}{c|c} \star & \star \end{array} \quad \begin{array}{l} P = \frac{2 \times T}{2} \\ P = T \end{array} \quad \begin{array}{l} P = \frac{2 \times T}{1} \\ P = 2T \end{array}$$

- Collapsing Pressure in alveoli is :
 - directly proportional to surface tension
 - and inversely proportional to radius of alveoli
- The smaller the sphere the more surface tension
 - Pressure in smaller alveolus greater

Surface tension

$$P \text{ (collapsing Pressure)} = \frac{2 \times T}{r}$$

(a) Pressure is greater in the smaller bubble



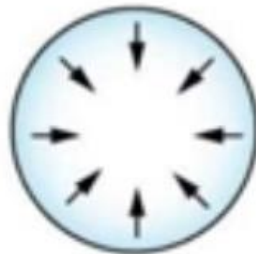
Larger bubble

$$r = 2$$

$$T = 3$$

$$P = (2 \times 3)/2$$

$$P = 3$$



Smaller bubble

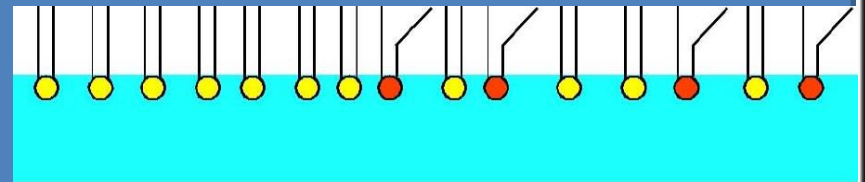
$$r = 1$$

$$T = 3$$

$$P = (2 \times 3)/1$$

$$P = 6$$

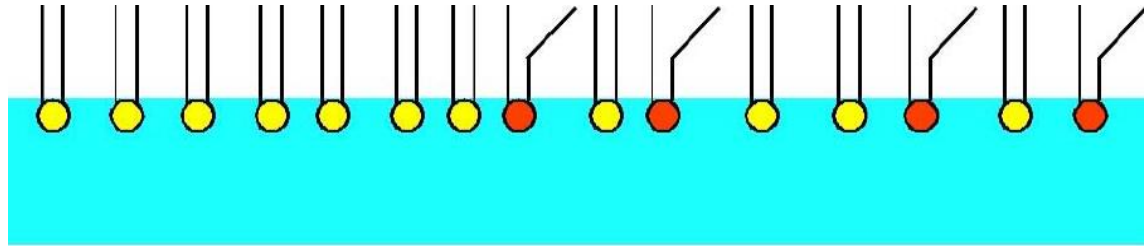
Lipids form a monolayer at the air-water interface



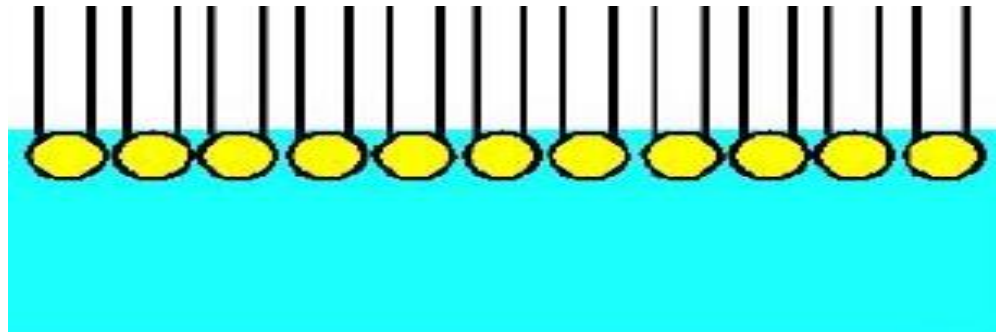
Surfactant

Will be discussed later on

Lipids form a monolayer at the air-water interface



Surface tension decreases as lipid monolayer is compressed



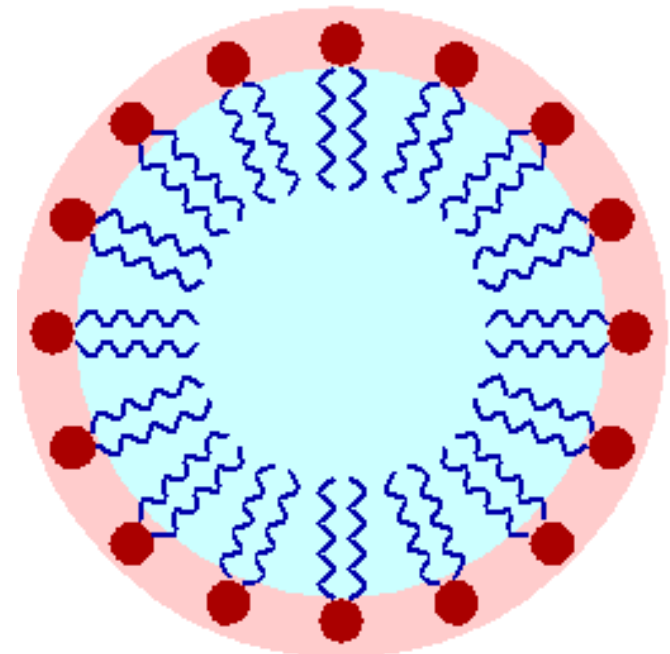
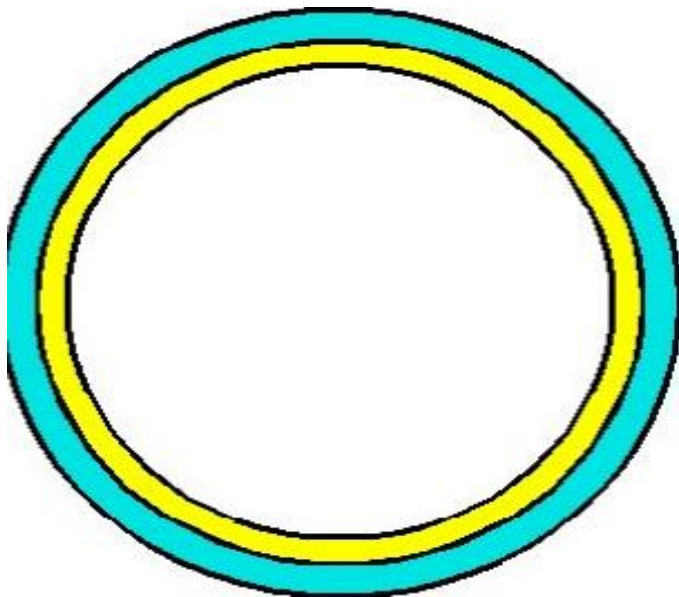
1. Alveoli are coated with lung surfactant in order to reduce the surface tension of water through:



a) It scatters among the fluid molecule decreasing the attraction between them.

b) It also spreads over the fluid preventing air-fluid interface.

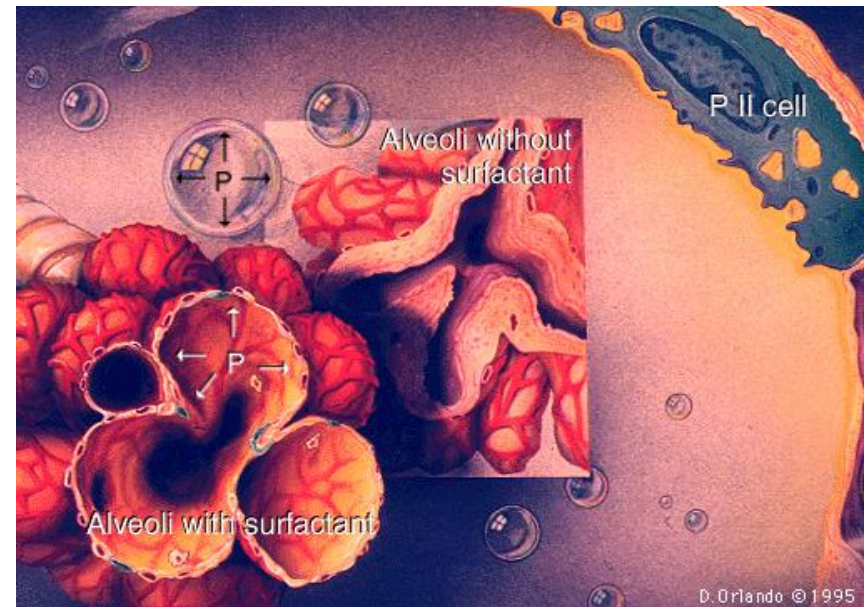
thus preventing collapse (atelectasis) upon exhalation and decreasing the force necessary to expand the alveoli upon inhalation



Lung Function in respiratory distress syndrome (RDS)

★ Syndrome indicates lack of surfactant!

- Reduction in FRC from 30 ml/kg, to as low as 4-5 ml/kg



Surfactant

- produced by alveolar type II cells

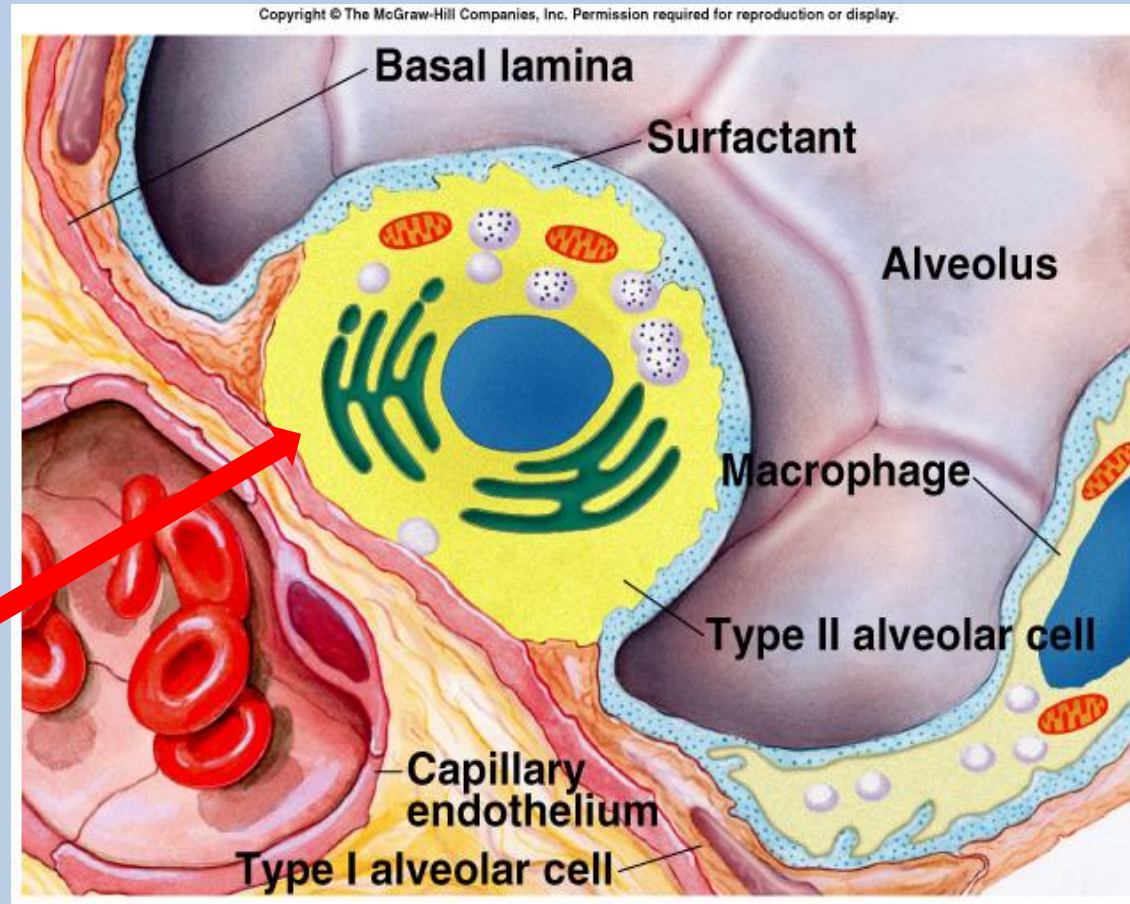
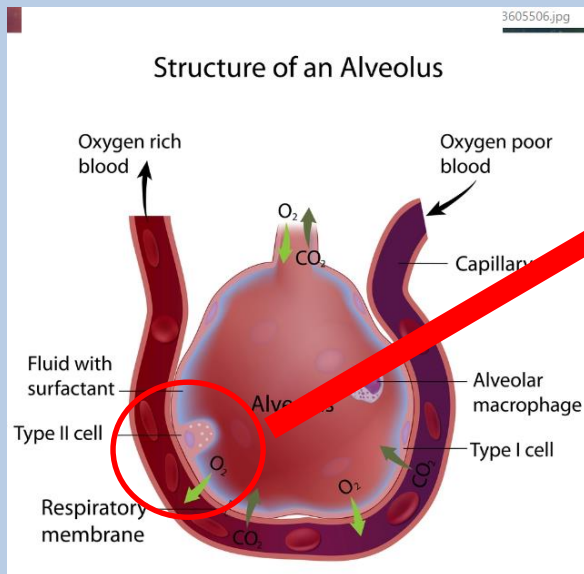


Figure 16.12

Endogenous Surfactant composition and functions

- **Major Lipids (~90%)**

- Saturated Phosphatidylcholine **DPPE** (**Lecithin**) 60-80% ★
- Unsaturated Phospholipids ✕
- Phosphatidylglycerol (**PG**) ~10%

- **Proteins (~10%)**

- SP-A **Immune Function* ★
Hydrophilic, Host defense
Surfactant homeostasis
- SP-B *Spreading of Lipid layer* ★
 - Hydrophobic, Spreading, ↓ surface tension
- SP-C *Spreading of Lipid layer* ★
 - Hydrophobic, Adsorption
- SP-D: ? Phagocytic function

Surfactant Composition

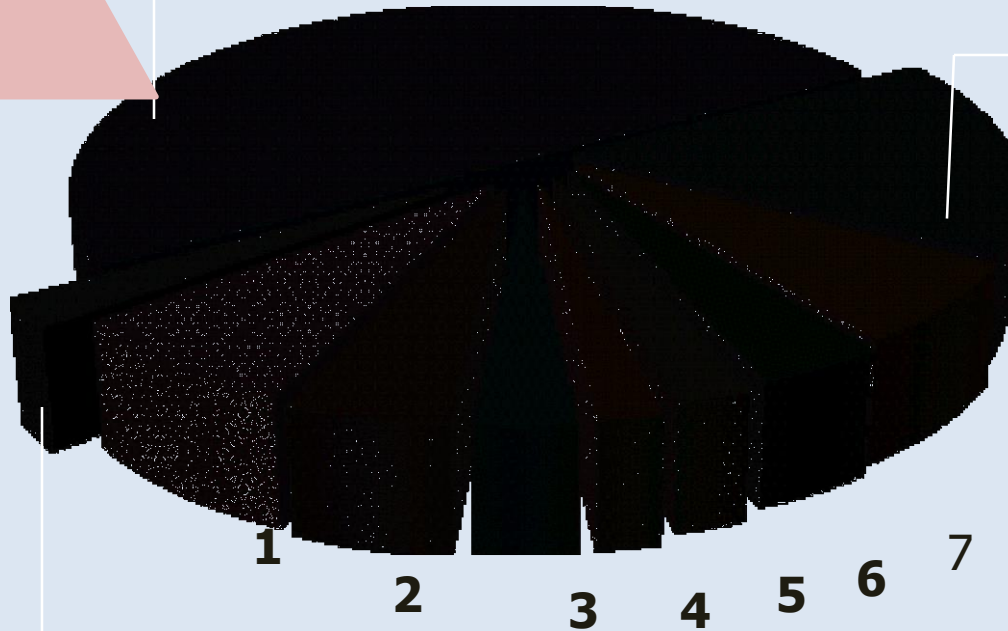
DPPC - dipalmitoylphosphatidylcholine 60%*

- *Reduces alveolar surface tension*

PG - phosphatidylglycerol

7%*

- *Promotes the spreading of surfactant throughout the lungs*



1. Serum proteins 10%
2. Other lipids 5%*
3. Other phospholipids 3%*
4. Phosphatidylinositol 2%*
5. Sphingomyelin 2%*
6. Phosphatidylethanolamine 4%*
7. Unsaturated Phosphatidylcholine 17%*

Prenatal diagnosis



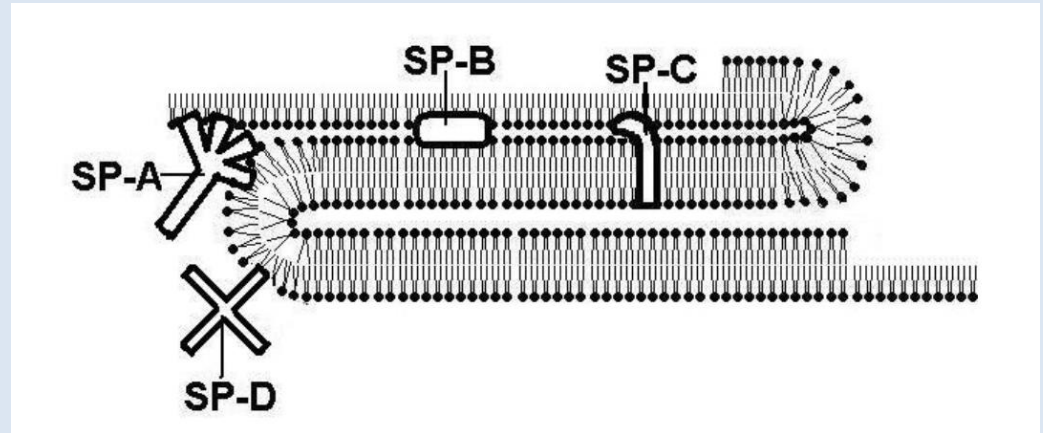
- Lecithin and sphingomyelin ratio in the amniotic fluid, if ratio is more than 2 indicates adequate lung maturity

** By molecular weight*

Surfactant proteins

Surfactant proteins are divided into 2 groups:

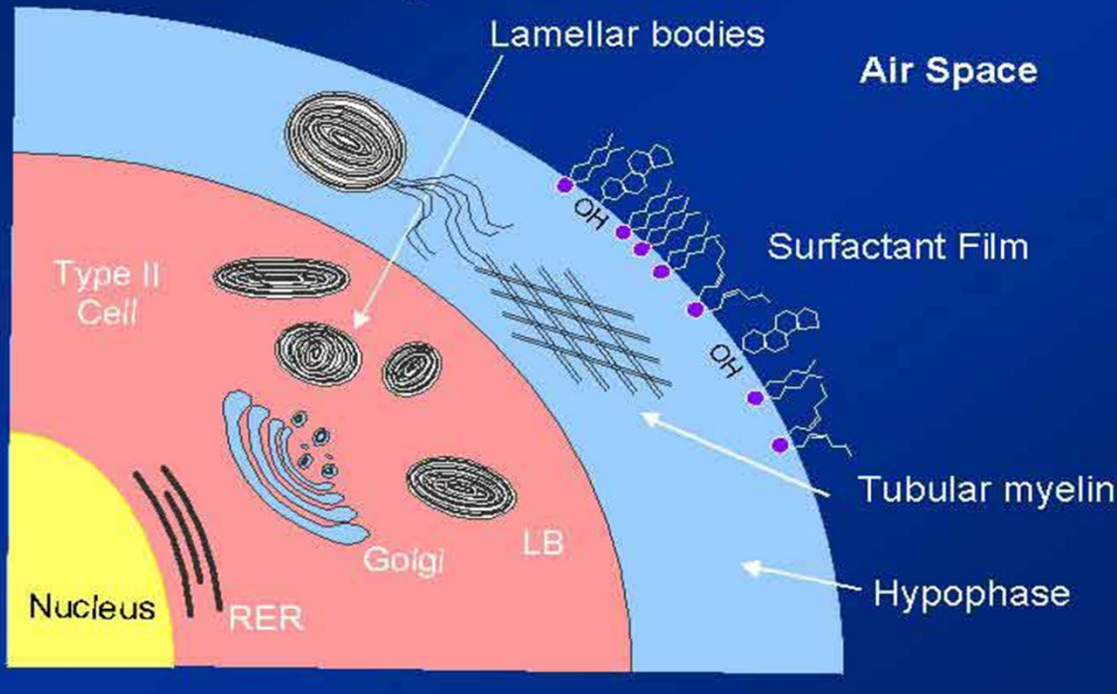
- **Large and water-soluble SP-A and SP-D proteins** ★
- **small, hydrophobic SP-B and SP-C proteins.** ★



Are of great importance to immune defense mechanisms of the lung
-ability to bind to bacteria, viruses and other pathogens
.....(**Mainly protein A**)
- well as to activate alveolar macrophages

Component

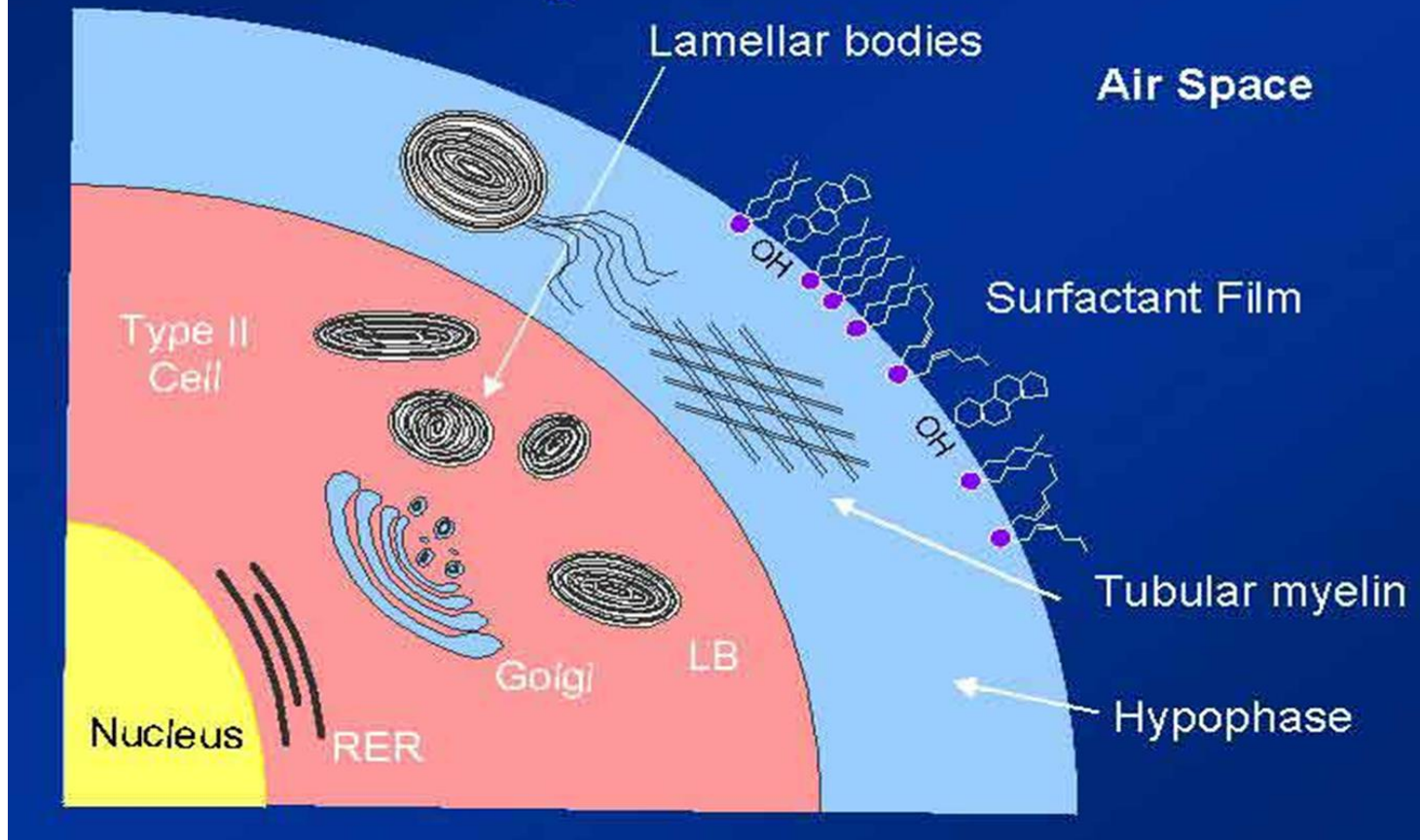
Surfactant Synthesis & Secretion



1-Lipid

- Synthesized in the smooth endoplasmic reticulum moved to Golgi apparatus

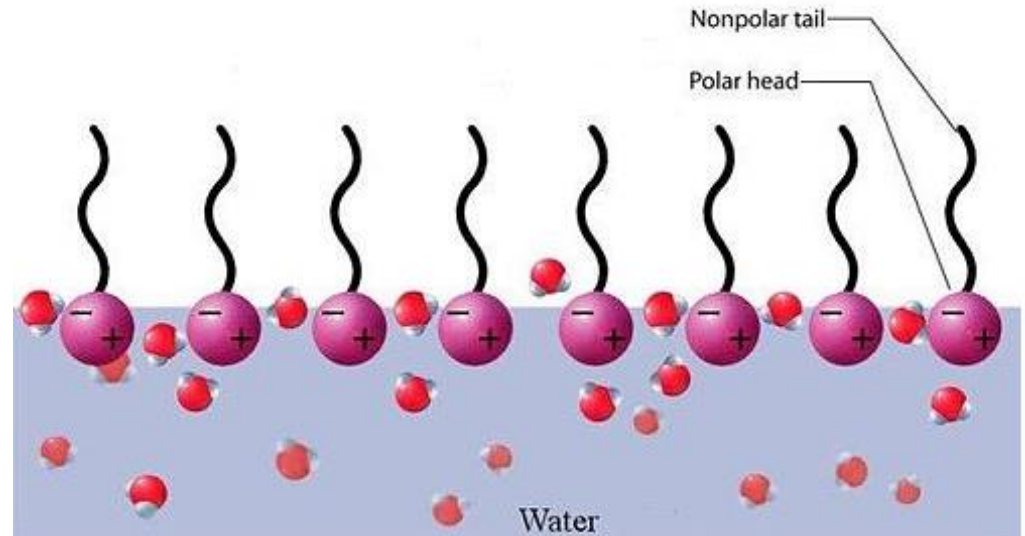
Surfactant Synthesis & Secretion



- **Surfactant** is synthesized by ***type II alveolar cells*** from fatty acids that either reach the lung from blood or formed (de novo) inside it. It is stored in organelles know as "***lamellar bodies***".

Component

Lipid

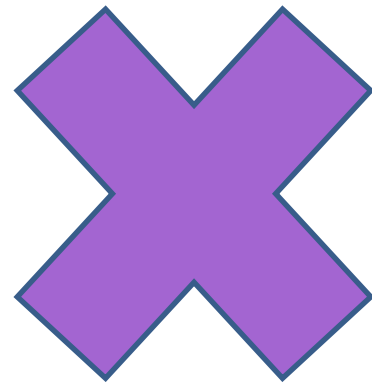


- The main constituent of the monolayer is
★
dipalmitoylphosphatidylcholine (DPPC), which

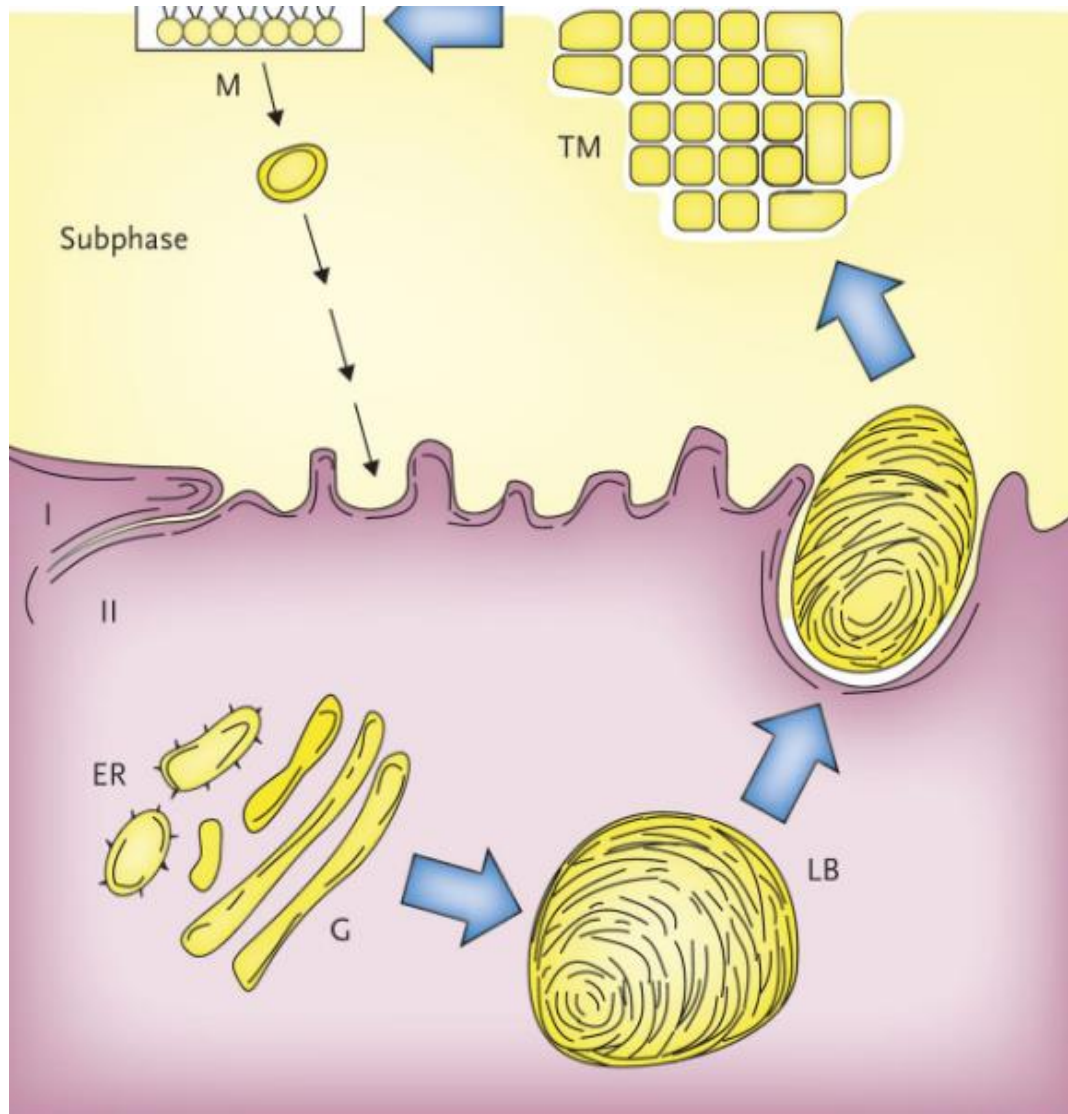
is a bipolar lipid (it has a hydrophilic 'head' and

a lipophilic 'tail')

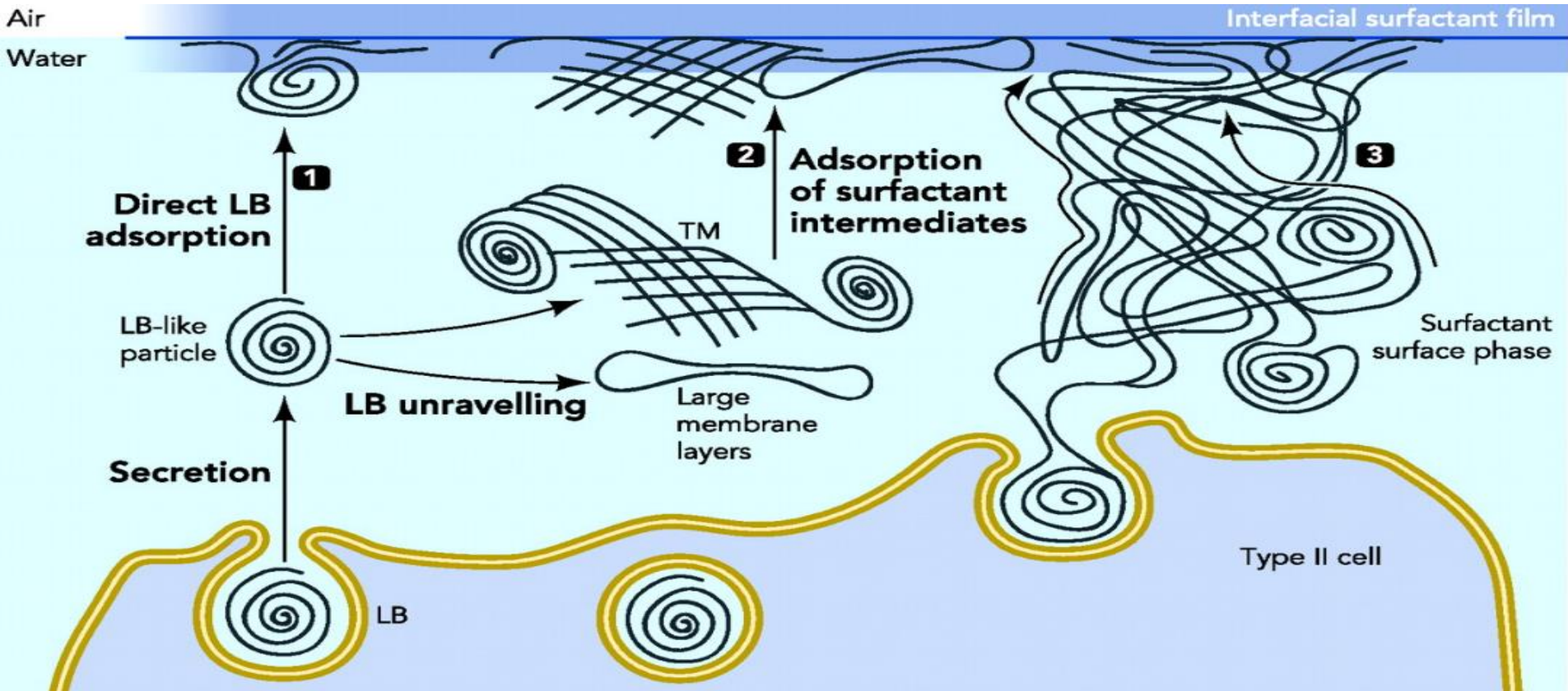
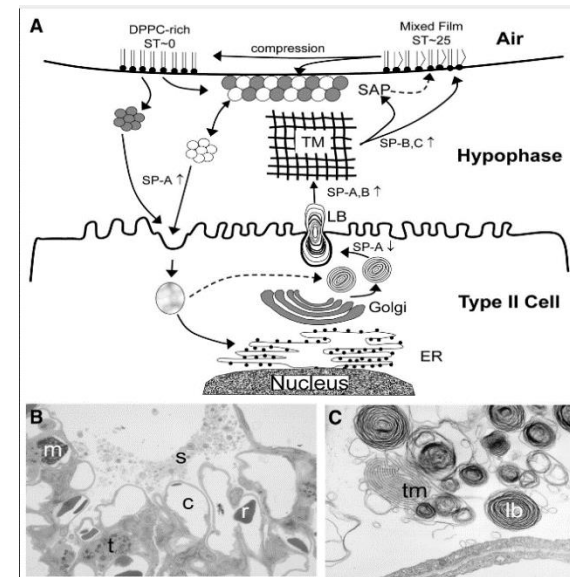
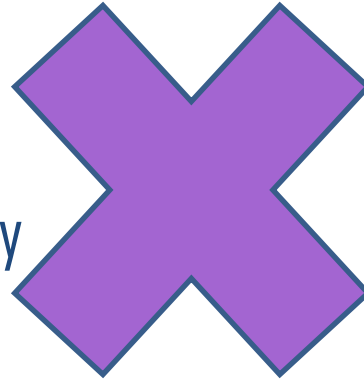
Surfactant synthesis



monomolecular surfactant



- Surfactant **Lipoprotein complex** that lowered the surface tension synthesized by Type II pneumocyte



Functions of surfactant:

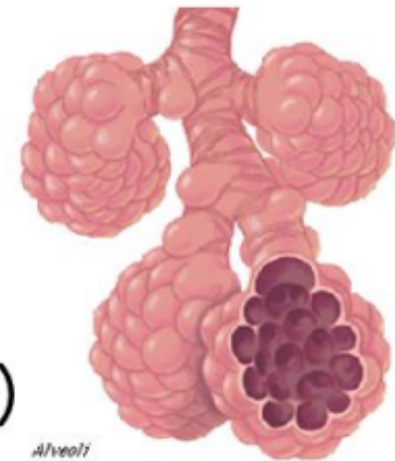


1-Decrease surface tension:

Roles of Lung surfactant

surfactant decreases surface tension

- \uparrow pulmonary compliance
- \downarrow alveolar collapse
- Respiratory distress syndrome (RDS)



Fetal lung maturity

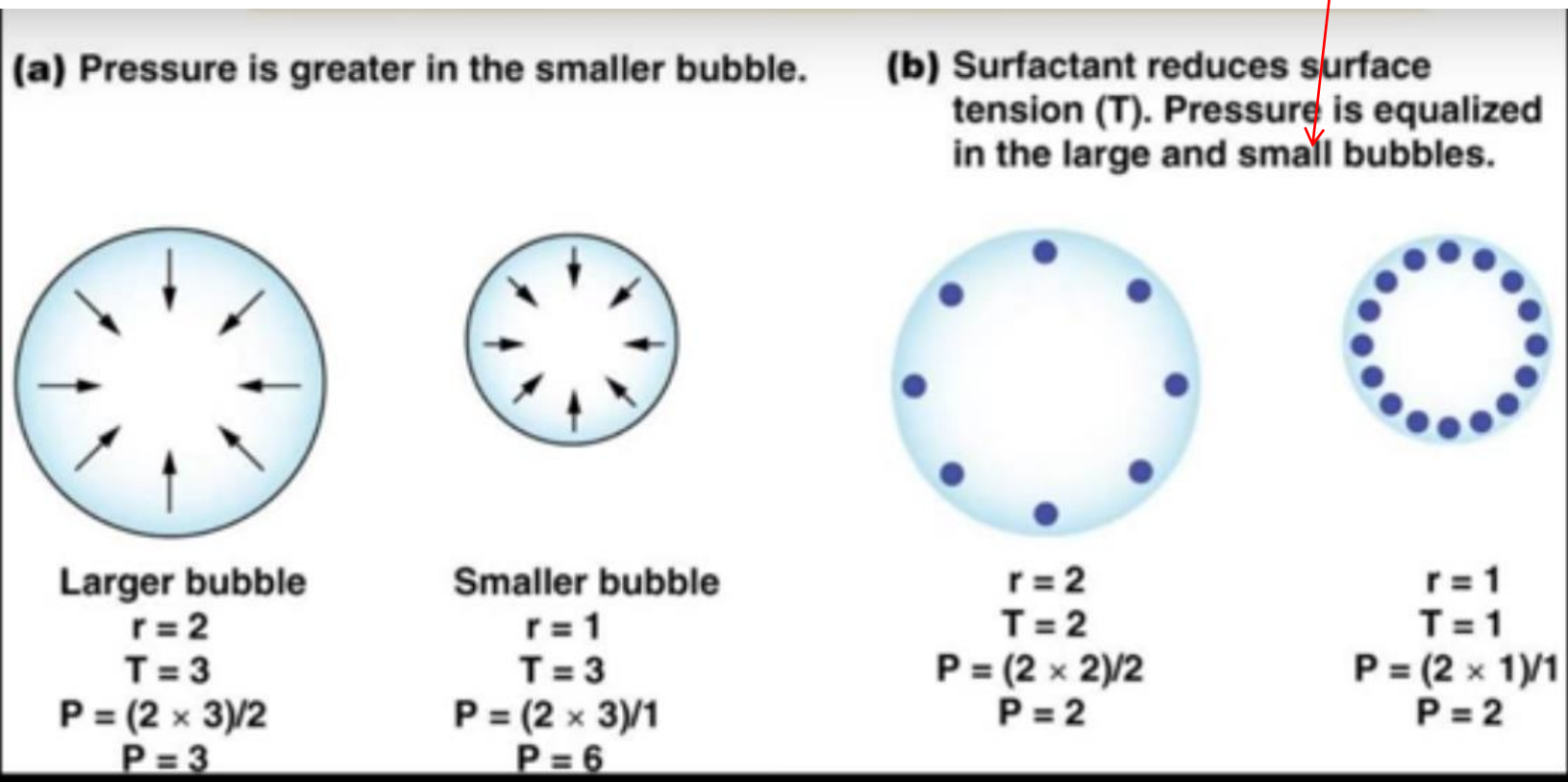


- L/S ratio $\xrightarrow{\text{Lecithin \& sphingomyelin}}$
- phosphatidylglycerol
- foam stability or shake test

L/S < 1.5	immature
L/S 1.5-1.9	intermediate
L/S \geq 2	lung maturity

Ventilation in the presence of surfactant

- Disrupts the surface tension & cohesion of water molecules
- Impact?
 - prevents alveoli from sticking together during expiration



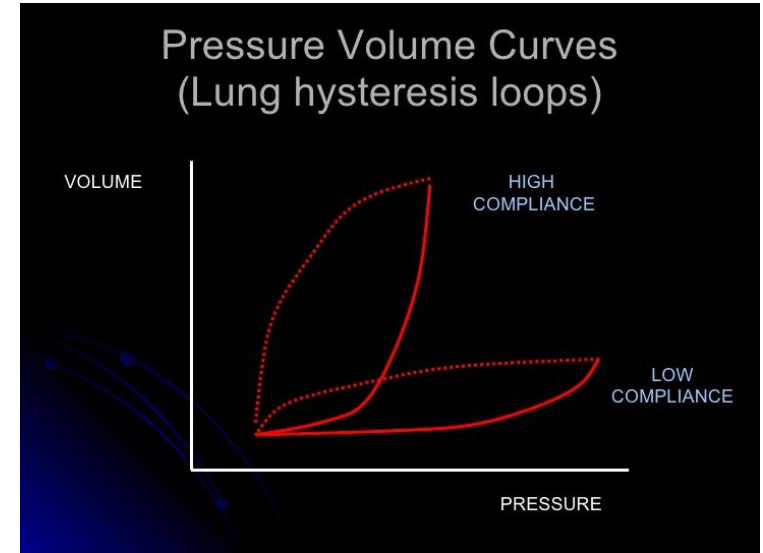
Functions of surfactant:

This decreased surface tension:

- Increase the lung compliance
 - Helps lung expansion during inspiration
 - stabilize the alveoli :

This protects the alveoli from

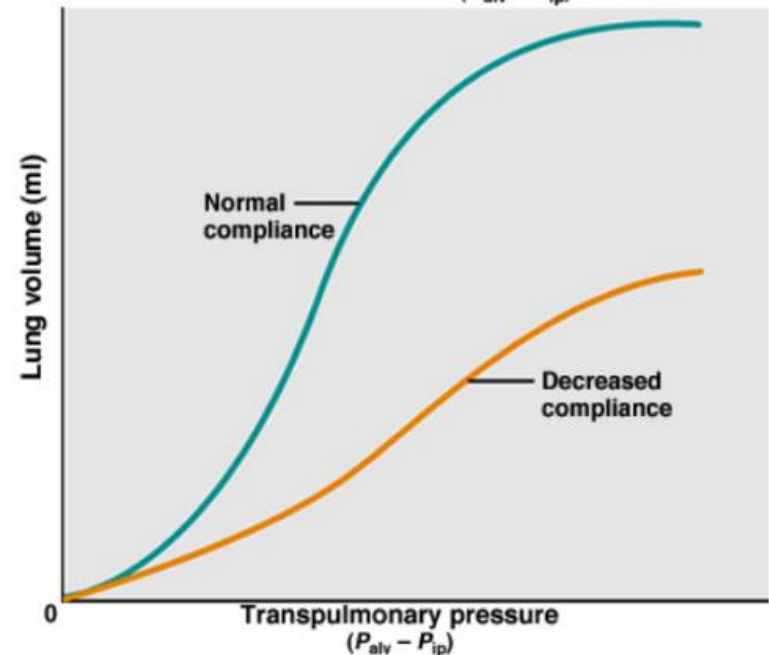
- ❑ Collapse during expiration
- ❑ over distention during inspiration
- ❑ Prevent collapse during expiration (atelectasis)



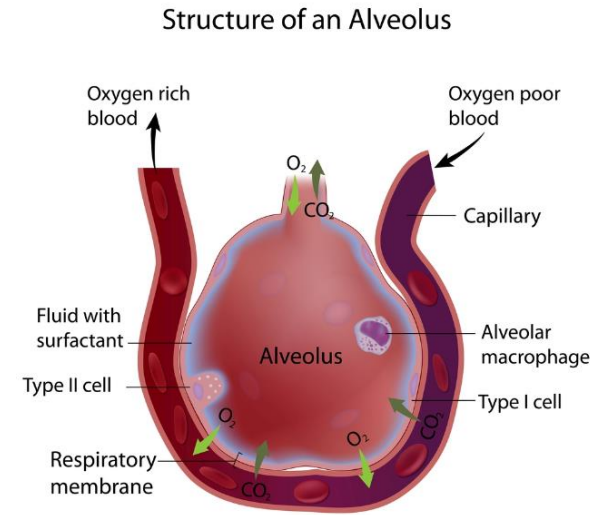
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Lung compliance


$$\text{Compliance} = \frac{\Delta \text{Lung volume}}{\Delta (P_{\text{alv}} - P_{\text{ip}})}$$



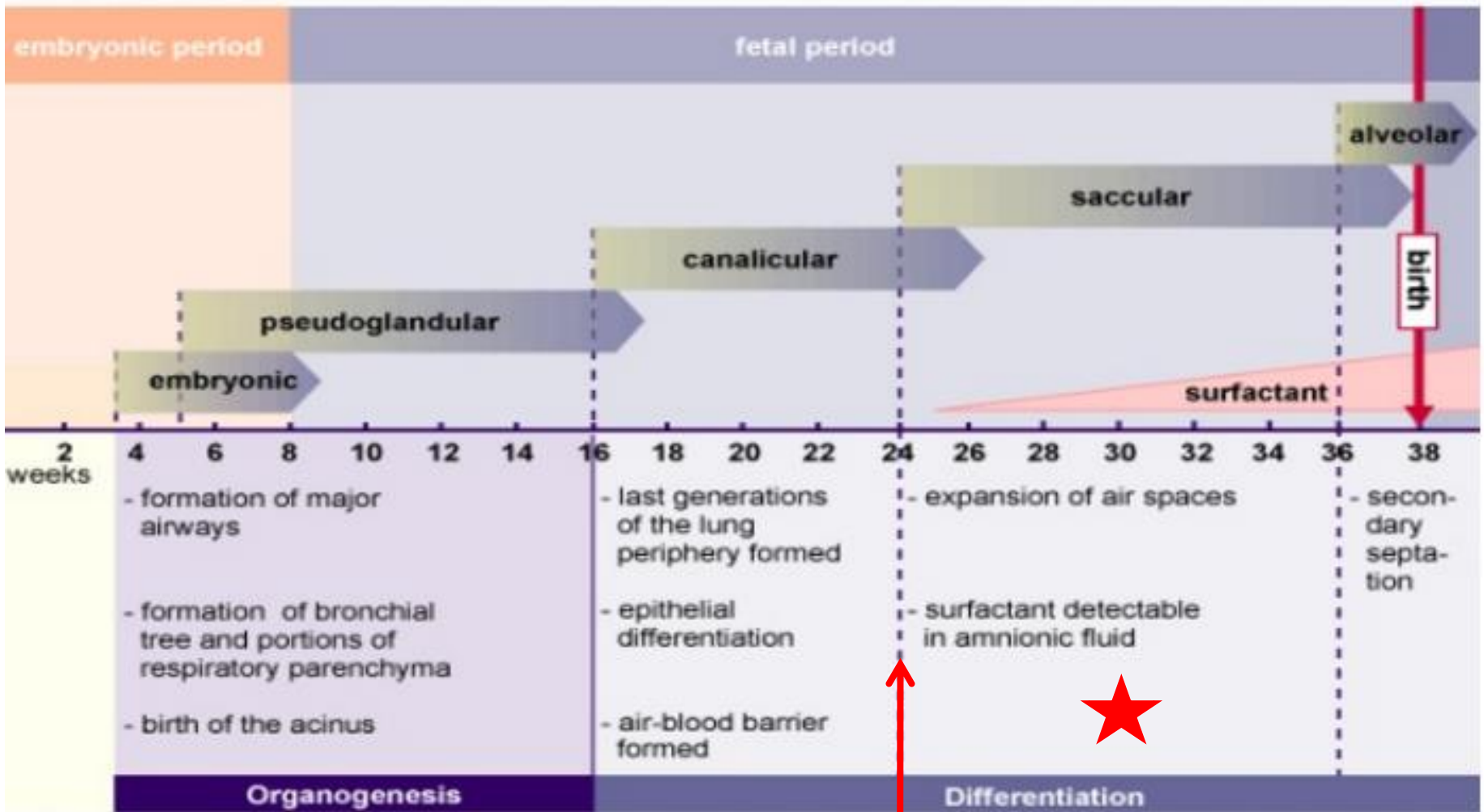
Functions of surfactant:

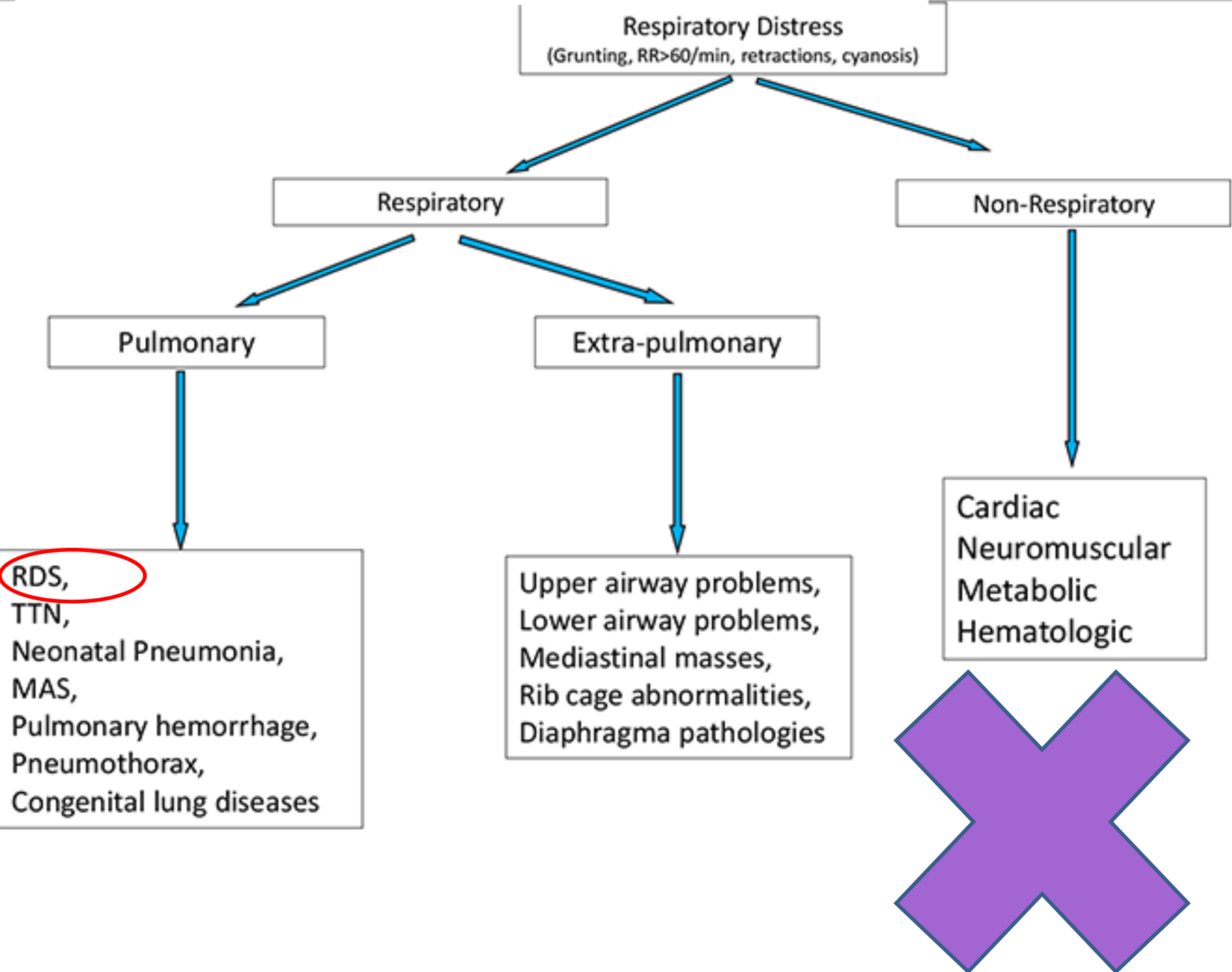


This decreased surface tension:

- Protects against pulmonary edema as it decreases the  filtration forces for the fluid from pulmonary capillaries into alveoli.

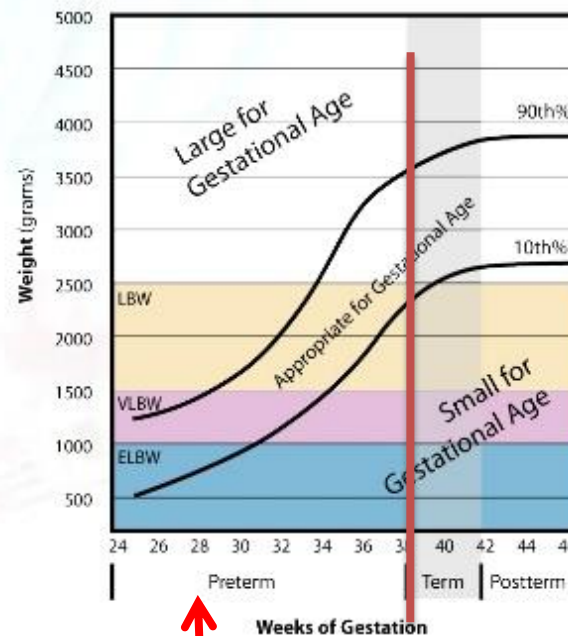
Phases of Lung Development





Case

- Baby born preterm at 28 week



Gestational Age

Classification of Size

- LGA** • SGA- small for gestational age-weight below 10th percentile
- AGA** • AGA-weight between 10 and 90th percentiles (between 5lb 12oz (2.5kg) and 8lb 12 oz (4kg)).
- SGA** • LGA-weight above 90th percentile
- IUGR-deviation in expected fetal growth pattern, caused by multiple adverse conditions, not all IUGR infants are SGA, may or may not be "head sparing"

Respiratory distress syndrome (RDS)

What Next ?

Preterm baby
Expected to
have RDS



CLINICAL MANIFESTATION



- ▶ Tachypnea
- ▶ Nasal flaring → Flow = $1/\text{radius}$ → so nares are lifted upward to increase their radius for better flow
- ▶ Intercostal, sternal recession
- ▶ Grunting; closure of glottis during expiration
- ▶ Cyanosis



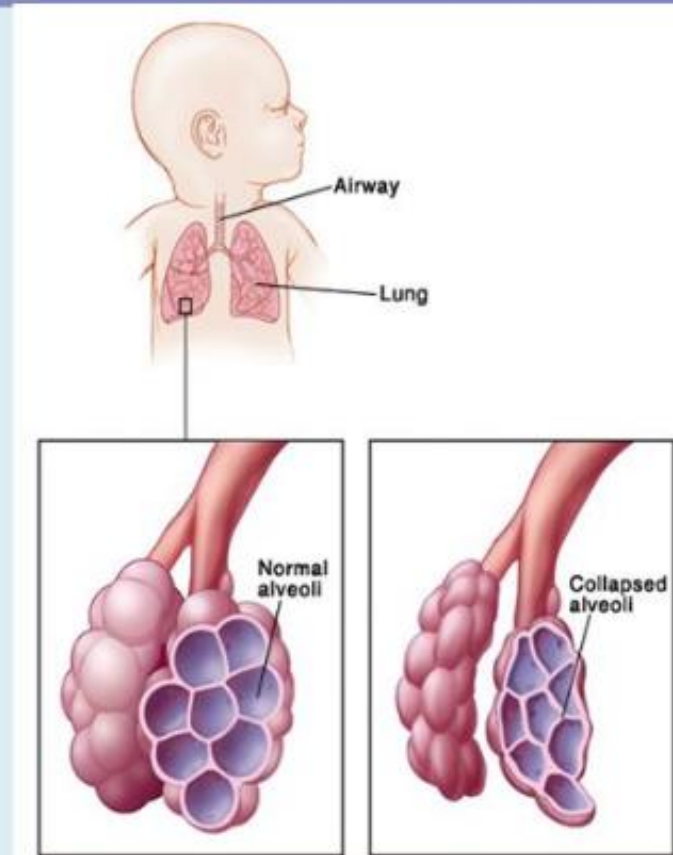
**These manifestations happen with all respiratory diseases*

DEFINITION • Acute lung disease of the newborn

Respiratory Distress Syndrome (RDS)

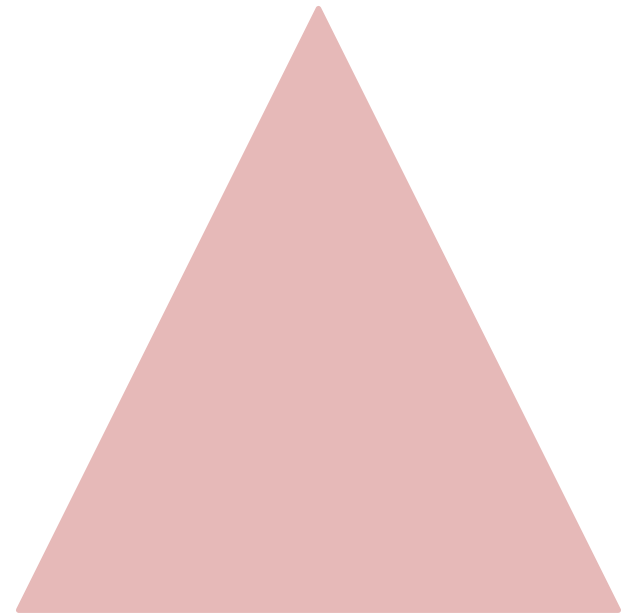
- Also called hyaline membrane disease.
- Most common cause of respiratory distress in preterm infants.
- Due to structural and functional immaturity of lungs.
 - Underdeveloped parenchyma
 - Surfactant deficiency
 - Type II pneumatocytes
- Results in decreased lung compliance, unstable alveoli

“Atelectasis”



pathophysiology

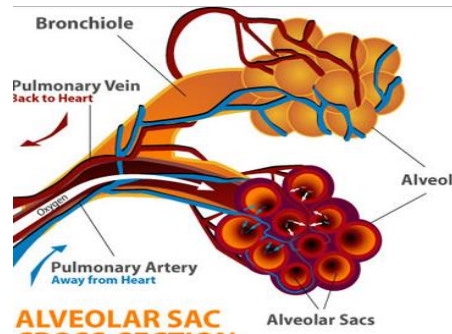
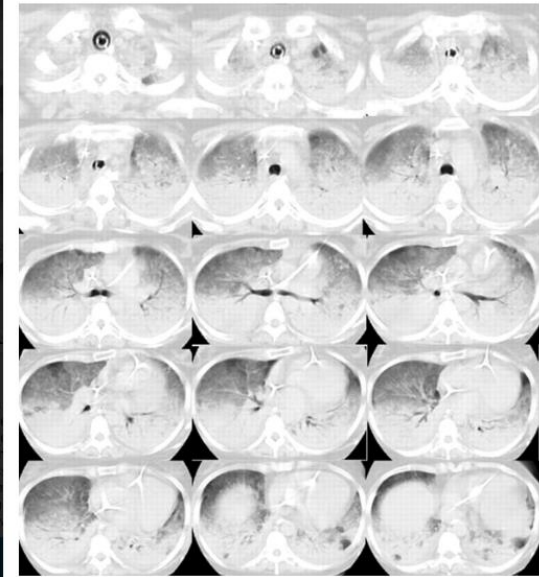
- Instability of terminal airspaces (difficult to expand during inspiration and atelectasis at expiration) due to elevated surface forces at liquid-gas interfaces (elevated surface tension)



Diminished surfactant :

- ★ ➤ Progressive Atelectasis
- ★ ➤ Loss of functional residual capacity
 - Small lungs and small tidal volume
- ★ ➤ Alterations in ventilation perfusion ratios
- ★ ➤ Uneven distribution of ventilation

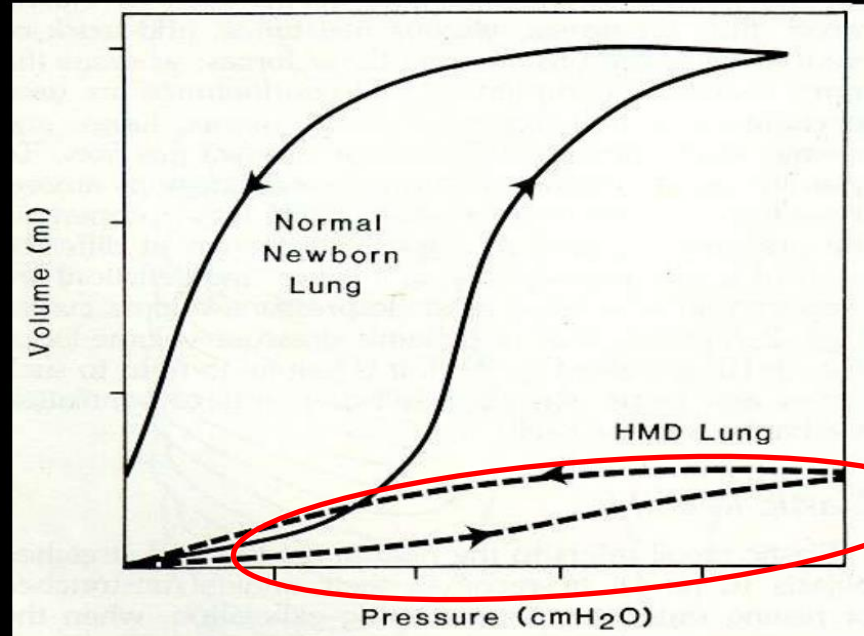
“V/Q mismatch due to collapsed alveoli”



Lung compliance in RDS

★ Lung Compliance is also reduced: from 1-2 to 0.2 - 0.5 ml/cmH₂O/kg

PRESSURE VOLUME LOOP



RDS: clinical picture

- At admission of the baby he has

- Cyanosis

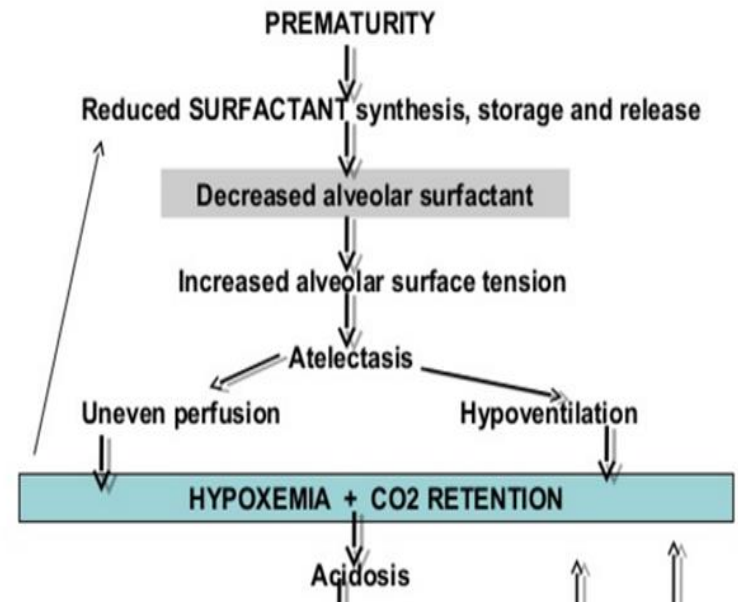
★ • ↓ Pulse Oximeter 75% (normal > 95%) For Saturation: O₂ attached to hemoglobin

Blood gas:

• ↓ PaO₂ = 45 mmHg (normal 80-108) → O₂ content in the serum

• ↓ Ph = 7.2 (normal 7.35-7.45) → Acidosis

• ↑ CO₂ = 65 mmHg (normal 35-45)



PREMATURITY

Reduced SURFACTANT synthesis, storage and release

Decreased alveolar surfactant

Increased alveolar surface tension

Atelectasis

Uneven perfusion

Hypoventilation

HYPOXEMIA + CO₂ RETENTION

Acidosis

Pulmonary Vasoconstriction

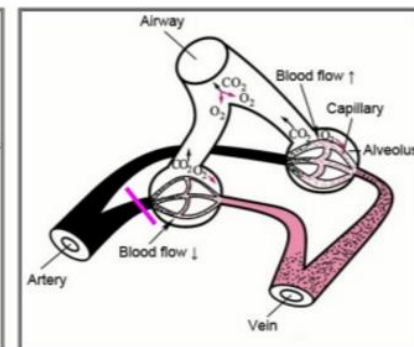
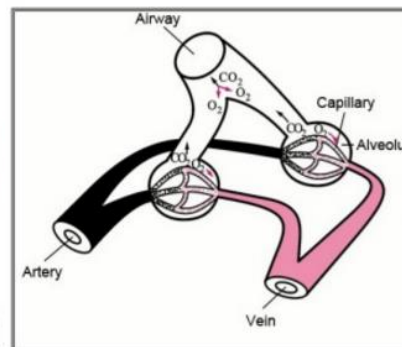
Pulmonary hypoperfusion

Increased
diffusion
gradient

Endothelial damage + Epithelial damage

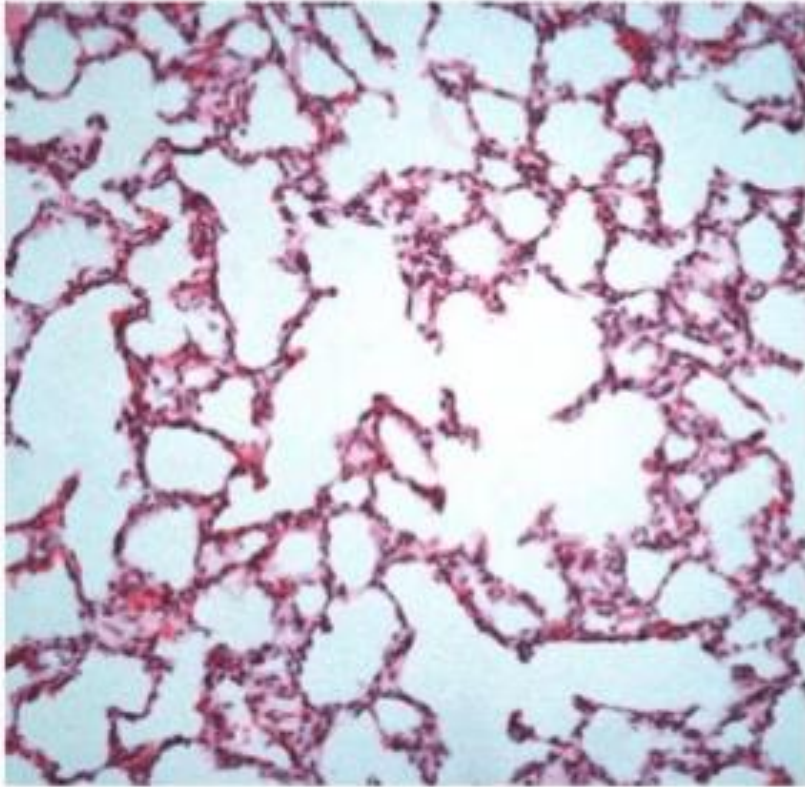
Plasma leak into alveoli

FIBRIN + NECROTIC CELLS
(HYALINE MEMBRANE)

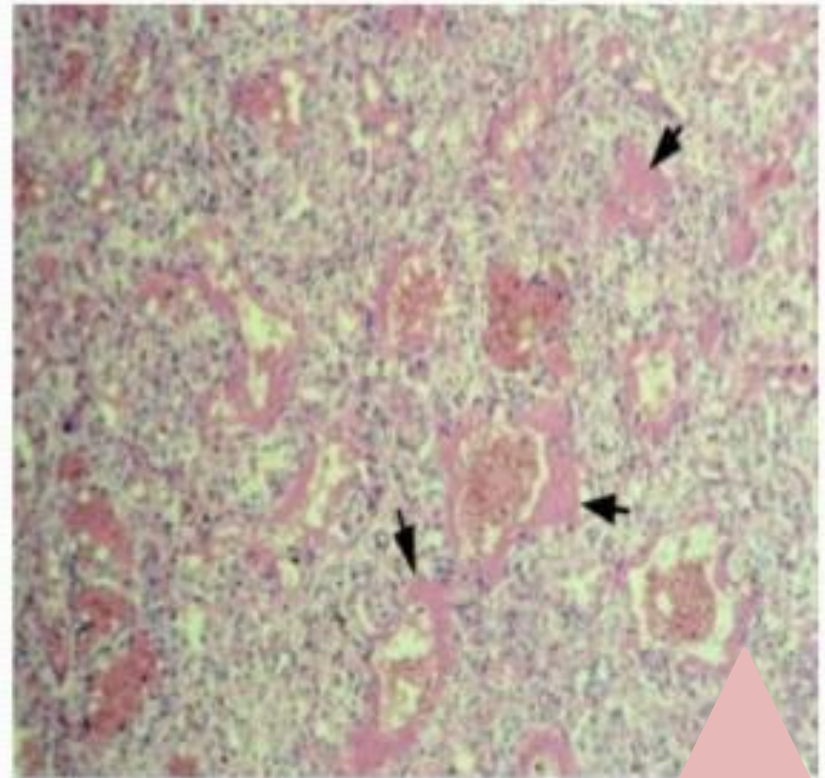


Lung hypo-perfusion
V/Q mismatch

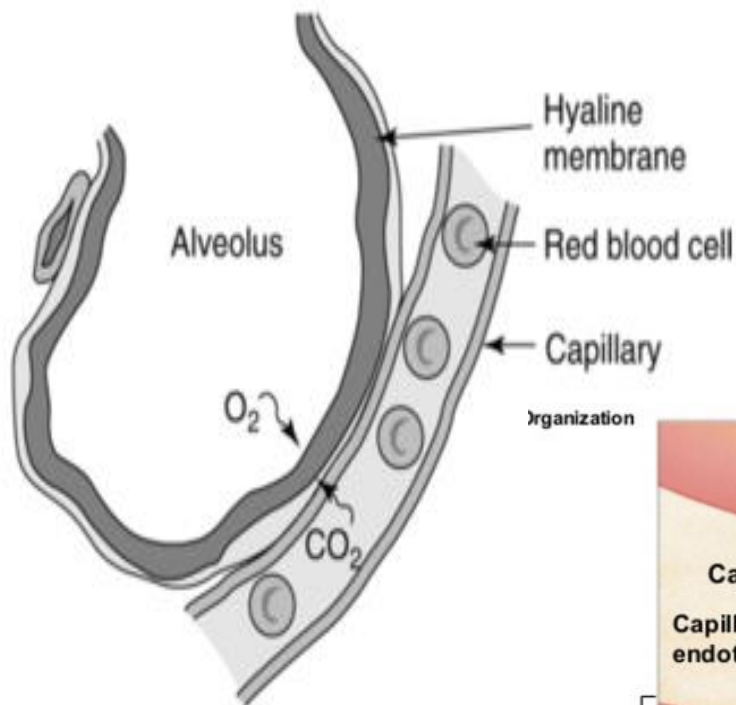
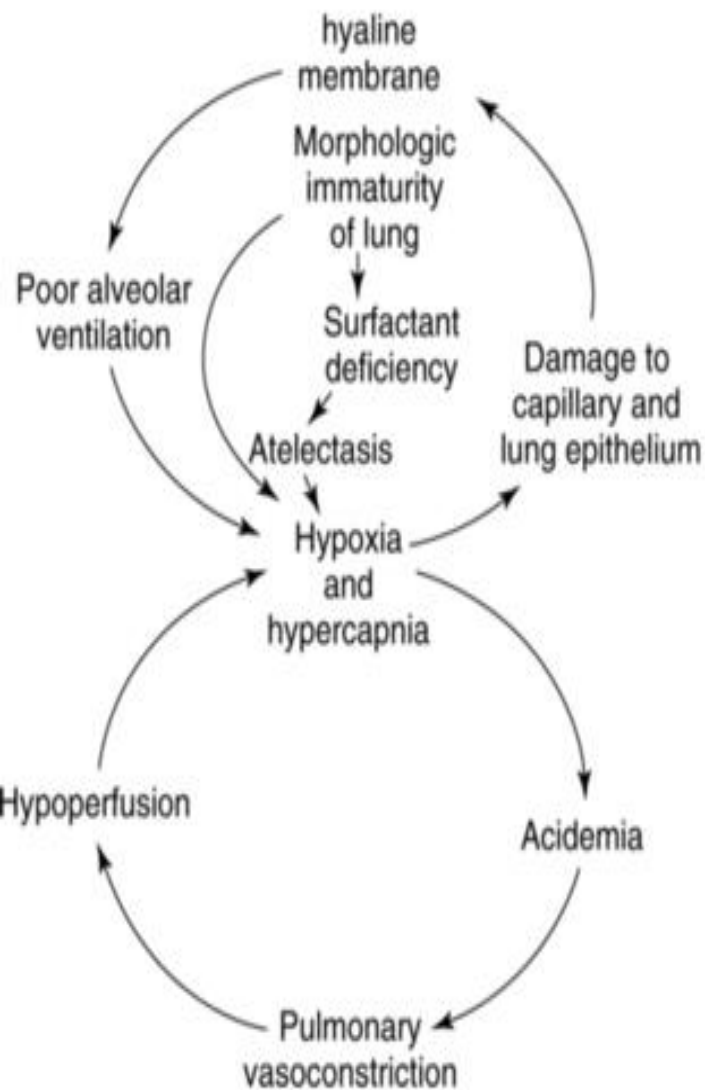
Normal Lung



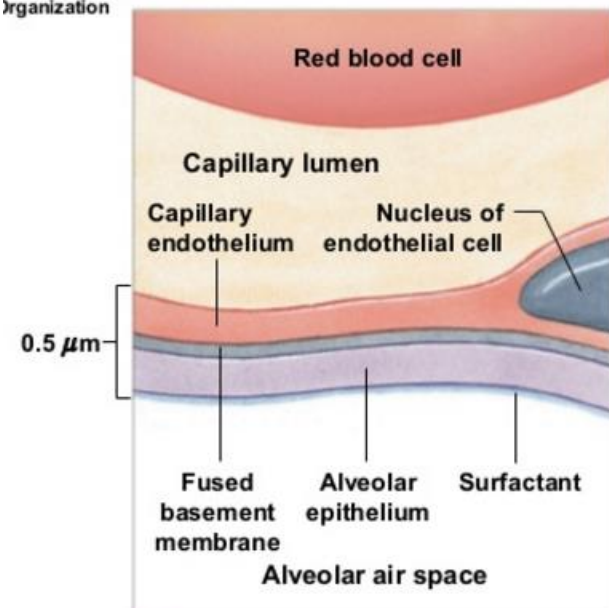
Hyaline Membranes



- Hyaline membrane- combination of sloughed epithelium, protein & edema.

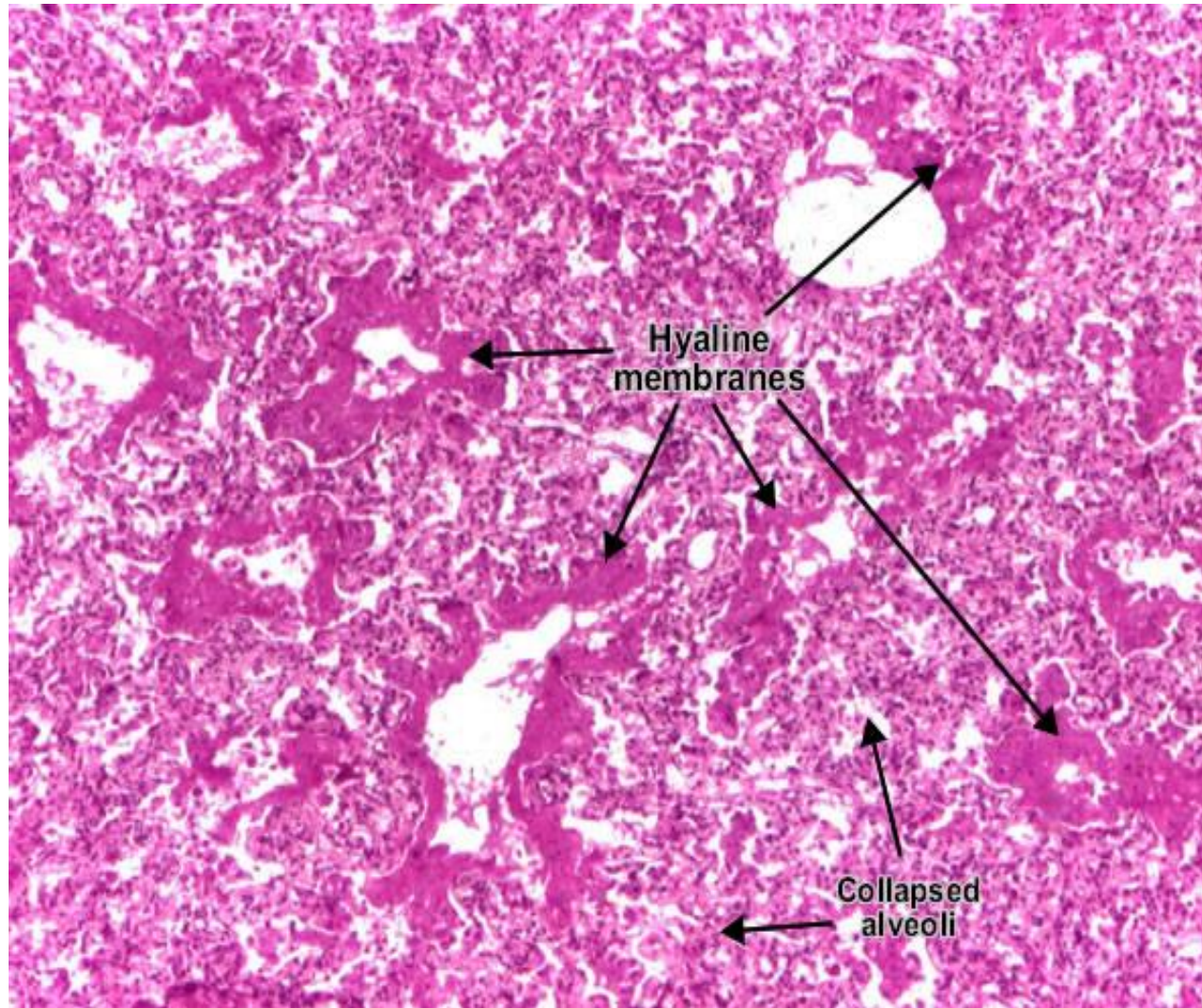
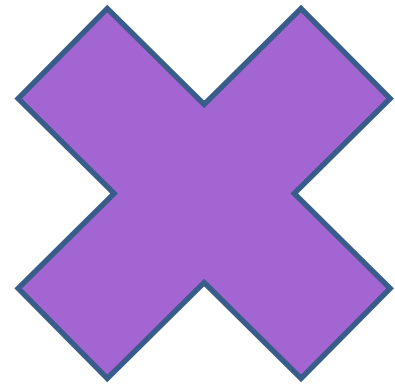


Organization

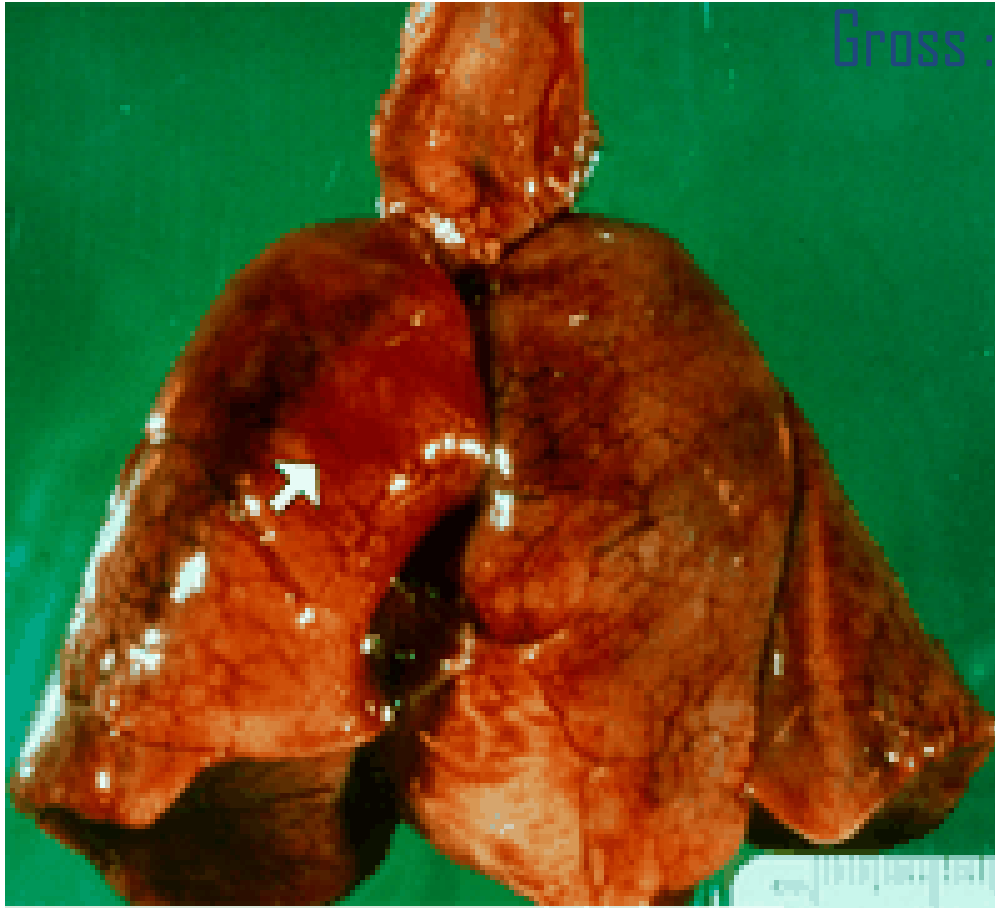


c The respiratory membrane, which consists of an alveolar epithelial cell, a capillary endothelial cell, and their fused basement membranes.

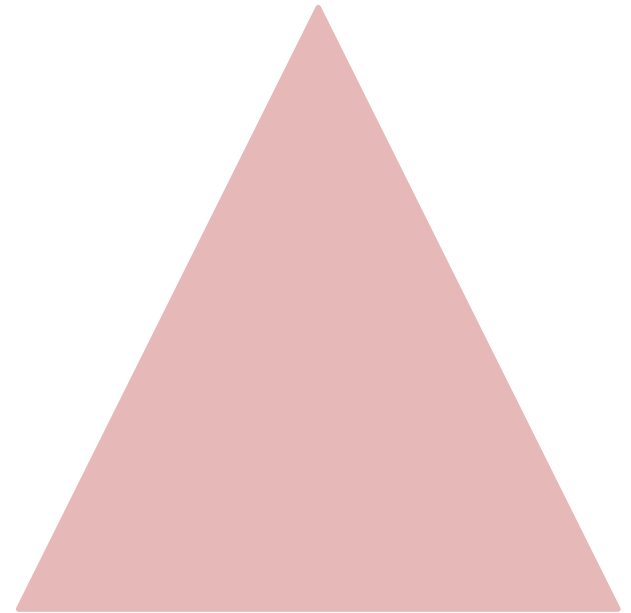
➤ Hyaline membrane- combination of sloughed epithelium, protein & edema.



- Hyaline membrane- combination of sloughed epithelium, protein & edema.



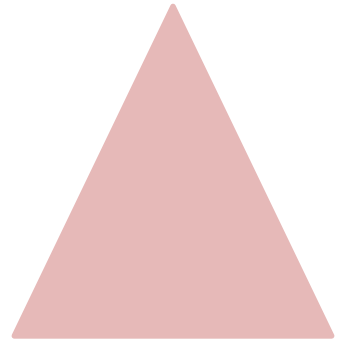
Gross : Lung firm, red, liverlike



- Photograph of an autopsy specimen demonstrates small atelectatic lungs with focal hemorrhage (arrow) visible on the pleural surface.

Incidence

Respiratory Distress Syndrome (RDS)



- Also known as Hyaline Membrane Disease (HMD)
- Commonest cause of preterm neonatal mortality
- RDS occurs primarily in premature infants; its incidence is inversely related to gestational age and birth weight

Gestational age	Percentages
Less than 28 wks	60-80%
32-36 wks	15-30%
37-39 wk	5%
Term	Rare

Nelson Textbook of Pediatrics, 18th Ed.

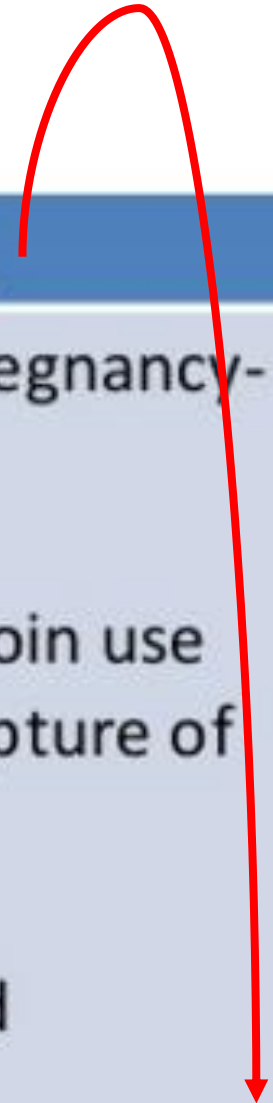


The more the baby is preterm the more risk of RDS there is



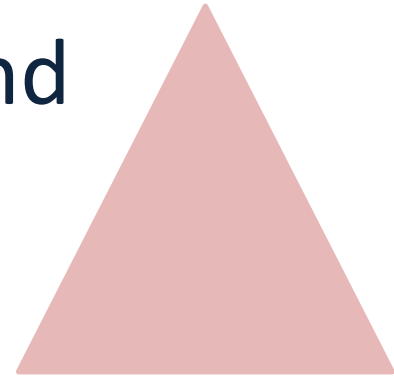
Risk Factors

<u>Increased Risk</u>	<u>Decreased Risk</u>
<ul style="list-style-type: none">• Maternal diabetes• multiple births• cesarean section delivery• perinatal asphyxia• cold stress• history of previously affected infants	<ul style="list-style-type: none">• Chronic or pregnancy-associated hypertension• maternal heroin use• prolonged rupture of membranes• antenatal corticosteroid prophylaxis <p>All of these are related to increased cortisol level in the fetus</p>

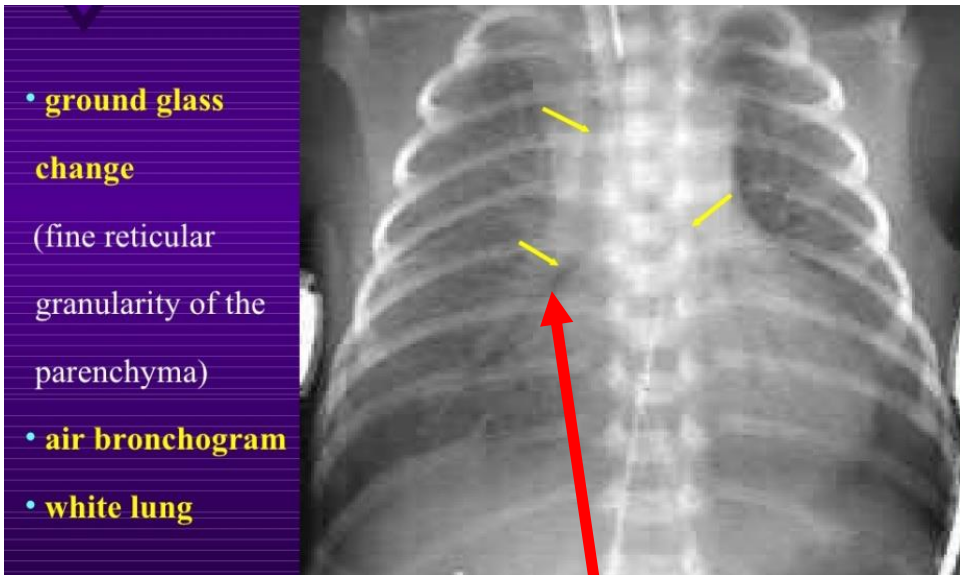


Just know that there is susceptibility
Details are not important!, only highlighted
things. *Saffar*

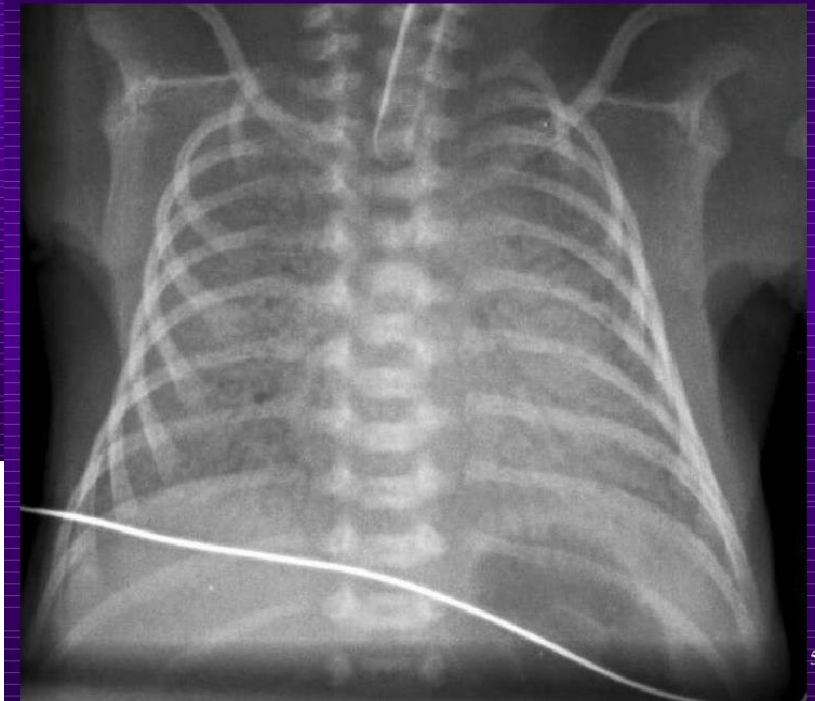
- Susceptibility to RDS is interaction between genetic, environmental and constitutional factors
- *Very preterm infants*
 - Common alleles predicts RDS: **SP-A** 642, Sp-B121, Sp-C 186 ASN.
- Term Infants: Loss of function mutation of **SP-B, SP-C**, phospholipids transporter ABCA3



Chest X-Ray



Severe RDS- white lung



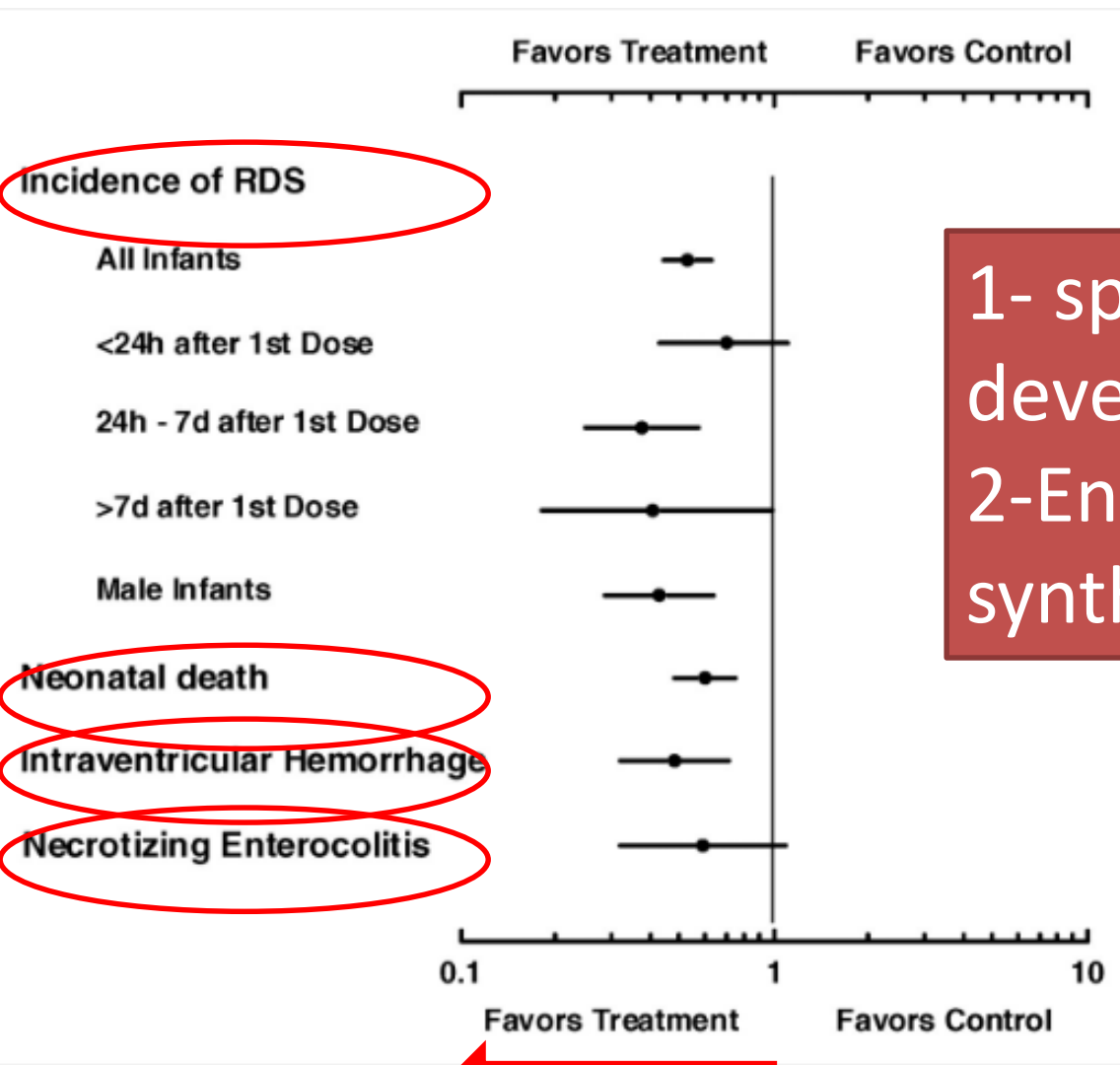
Due to closed alveoli

➤ Chest radiograph: air bronchogram, reticular/ ground-glass appearance after 6-12 hrs to full opacity later on.

Prevention

- ★ • Prevention of prematurity
 - Antenatal corticosteroid therapy
 - Dexamethasone or betamethasone
 - ↓ RDS morbidity and mortality
 - PS prophylactic therapy

Antenatal Corticosteroid Effects



1- speed up lung development
2- Enhance surfactant synthesis



Less than 1 favors treatment



Specific

RDS - Treatment

- Oxygen
 - CPAP
 - Mechanical ventilation
 - Surfactant replacement
 - Supportive Care
-



Management
Of
RDS...!!!

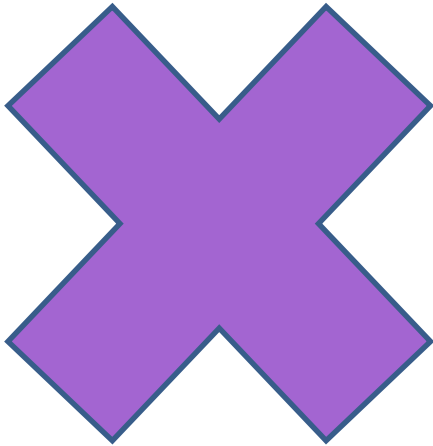


CPAP in RDS: How does it work ?

- Diminishing atelectasis
- Improving Functional residual capacity
- Correcting ventilation-perfusion abnormalities
- Decreasing pulmonary edema
- Reducing intrapulmonary shunting



PS replacement therapy



PS

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Antenatal steroid and Surfactant goes hand in hand



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Le Fin.

"je pense donc je suis"

Descartes

Omar Saffar