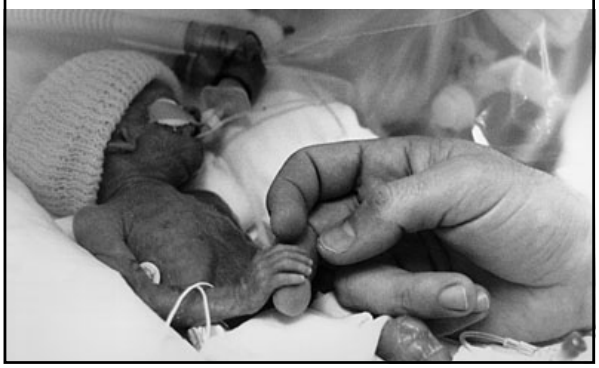
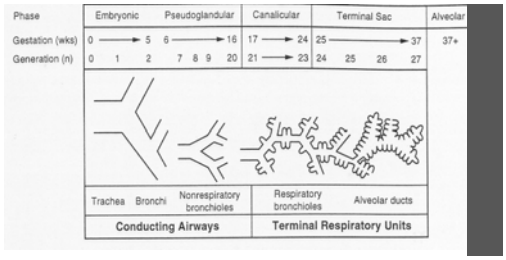
Respiratory Distress Syndrome



Stages of Lung Development



Lung Development

5 Stages of Embryogenesis

Embryonic Period **26 days to 6 weeks**	***Development of major airways***
Pseudoglandular Period **6 to 16 weeks**	***Development of airways to terminal bronchioles***
Canalicular Period **16 to 28 weeks**	***Development of acinus & vascularization***
Saccular Period **26 to 36 weeks**	***Subdivision of saccules by secondary crests***
Alveolar Period **36 weeks to term**	***The appearance of alveoli*** ***Mature surfactant levels***
Microvascular maturation **– Birth to 2 years**	

Lung Development

- **5 Stages of Lung Development**
  - Embryonic – *26 days to 6 weeks*
  - Pseudoglandular – *6-16 weeks*
  - Canalicular - *16-28 weeks*
  - Saccular - *26-36 weeks* ← **Our Patients**
  - Alveolar – *36 weeks to term*
  - Microvascular maturation – *birth to 2 years*
  - Simple growth – *1 to 18 years*

Respiratory Distress Syndrome (RDS)

- "Respiratory distress syndrome of the newborn", also known as hyaline membrane disease (HMD), is a syndrome caused in premature infants by developmental insufficiency of surfactant production and structural immaturity in the lungs.

Respiratory Distress Syndrome (RDS)

Frequency:

- **In the US:** RDS occurs in approximately 40,000 infants each year (1-2% of newborn infants or in 14% of infants weighing less than 2500 g).
- The incidence of RDS increases from 5% at 35-36 weeks to 65% at 29-30 weeks of gestation.
- The incidence of RDS is altered by antenatal maternal glucocorticoid use, as follows:
  - < 30 weeks of gestation, rates are 60% without glucocorticoid therapy versus 35% with antenatal glucocorticoid therapy.
  - 30 to 34 weeks of gestation, rates are 25% without glucocorticoid therapy versus 10% with antenatal glucocorticoid therapy.
  - > 34 weeks of gestation, the overall incidence is about 5%.

Respiratory Distress Syndrome (RDS)

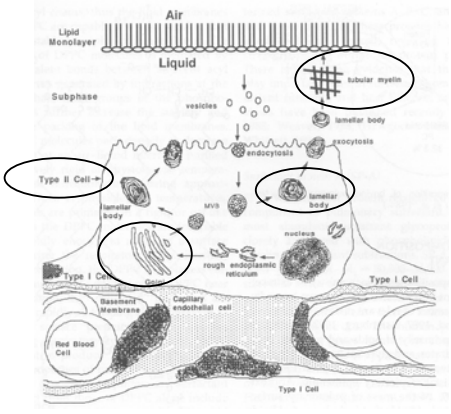
Pathophysiology:

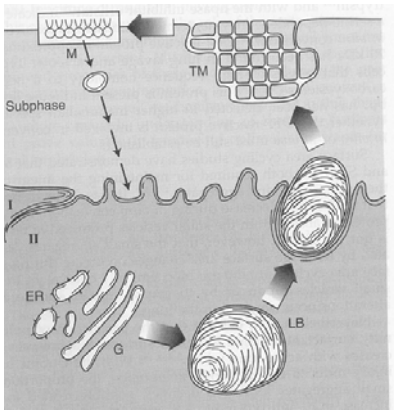
- RDS is the result of anatomic pulmonary immaturity and a deficiency of surfactant.
- Pulmonary surfactant synthesis, in type II pneumocytes, begins at 24-28 weeks of gestation, and gradually increases until full gestation.
- Pulmonary surfactant decreases surface tension in the alveolus during expiration, allowing the alveolus to remain partly expanded, thereby maintaining a functional residual capacity.

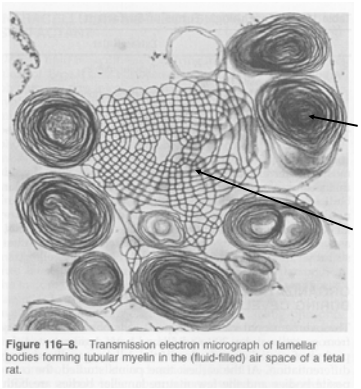
Respiratory Distress Syndrome (RDS)

Surfactant composition

- Phospholipids 80%
  - Phosphatidylcholine 80%
- Proteins 10%
  - SP-A, B, C, D
- Neutral lipids 10%



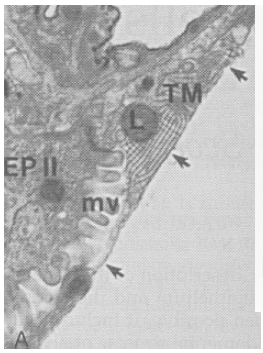




Lamellar Bodies

Tubular Myelin

Figure 116–8. Transmission electron micrograph of lamellar bodies forming tubular myelin in the (fluid-filled) air space of a fetal rat.



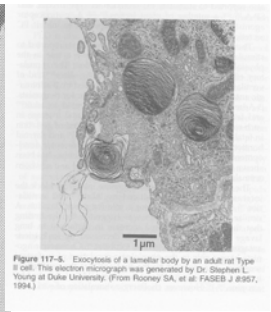


Figure 117–5. Exocytosis of a lamellar body by an adult rat Type II cell. This electron micrograph was generated by Dr. Stephen L. Young at Duke University. (From Rooney SA, et al: FASEB J 8:957, 1994.)

Tubular Myelin

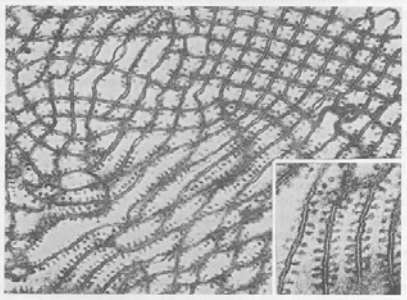


Figure 116–9. High-magnification transmission electron micrograph of tubular myelin. Regularly spaced globular profiles on short stalks that decorate the lipid bilayers are probably SP-A (inset shows a section parallel to the tubular structure at higher magnification). (Courtesy of C. Kuhn III, MD.)

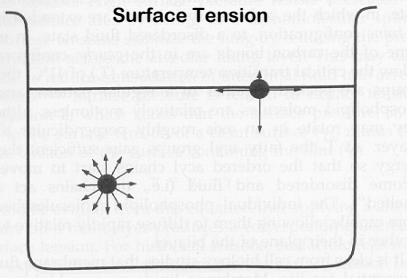
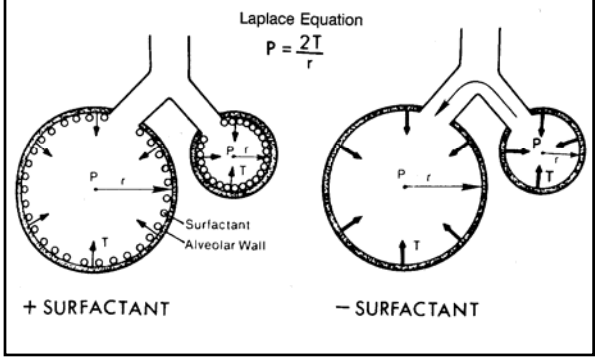
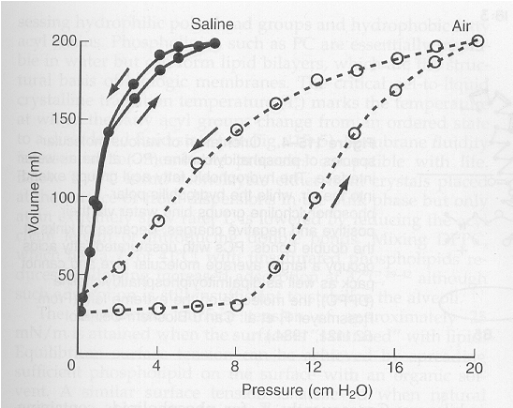


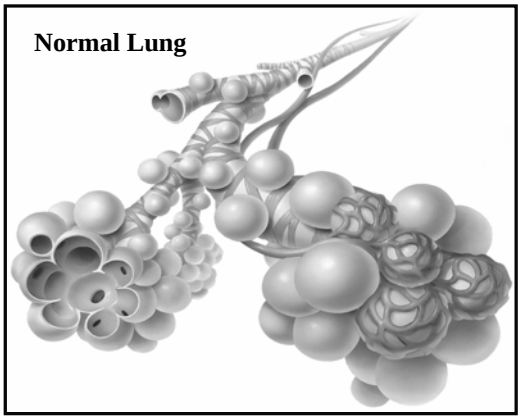
Figure 115–3. Diagrammatic representation of surface tension. A molecule of water within the bulk phase is attracted by all molecules surrounding it, but molecules of water at the surface experience a net attraction into the interior. (From Possmayer F, et al: Can J Biochem Cell Biol *62*:1121, 1984.)

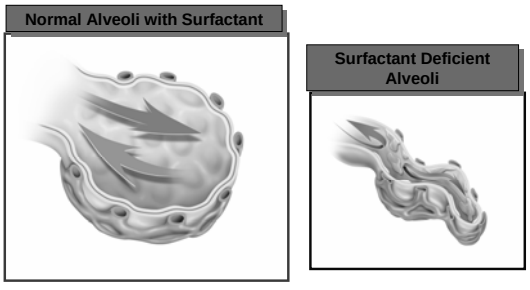
Surfactant function and metabolism




Saline
Air
200
150
100
50
Volume (ml)
0
4
8
12
16
20
Pressure (cm H_2O)

Normal Lung




Normal Alveoli with Surfactant
Surfactant Deficient Alveoli

Respiratory Distress Syndrome (RDS)

Clinical Signs & Symptoms:

- The clinical presentation of expiratory grunting (due to partial closure of glottis), tachypnea, subcostal and intercostals retractions, nasal flaring, and cyanosis usually manifests in the first few hours and almost always before 8 hours of age.
- If symptoms do not develop until after 8 hours of normal breathing, consider other causes including infection causes
- On auscultation, air movement is diminished despite vigorous respiratory effort.

Respiratory Distress Syndrome (RDS)

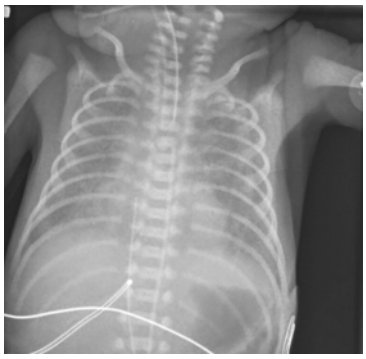
Clinical Signs & Symptoms:

- Cyanosis and hypoxia frequently become severe.
- Tachypnea, with respiratory rate greater than 60 breaths per minute, develops early.
- Functional residual capacity and pulmonary compliance are greatly reduced.
- A mixed respiratory and metabolic acidosis usually develops.
- Arterial blood gas studies show hypoxemia, hypercapnia, and respiratory acidosis.
- Hypoglycemia, hyperkalemia, and hypocalcemia are also common

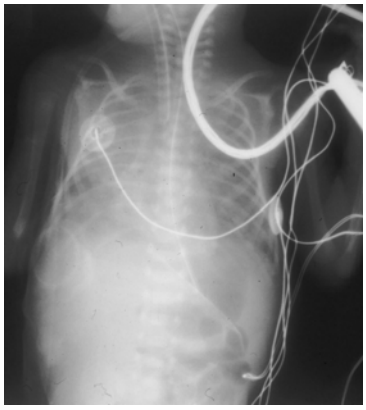
Respiratory Distress Syndrome (RDS)

Clinical Signs & Symptoms:

- Increased pulmonary vascular resistance develops because of a noncompliant lung, hypoxia, and acidosis.
- This effect increases the right-to-left shunt through a patent ductus arteriosus (PDA).
- Perfusion of atelectatic air spaces and uneven distribution of inspired air result in a ventilation-perfusion mismatch
- Typical X-ray shows atelectasis, common term is “ground glass” appearance



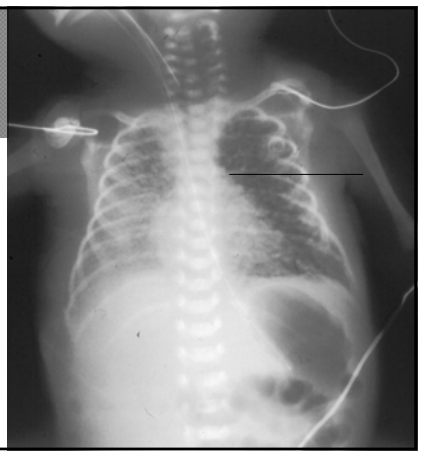
Mild HMD



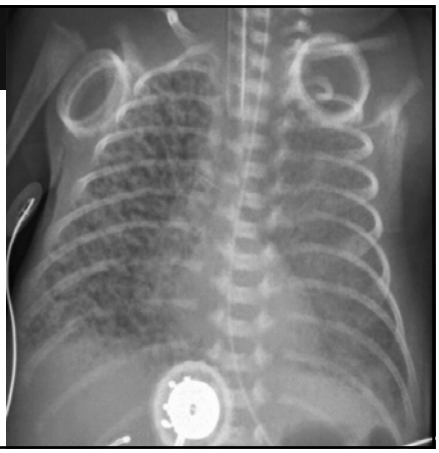
Severe HMD

Severe HMD with PIE –

On HFOV



RDS with Severe PIE



Respiratory Distress Syndrome (RDS)

Clinical Signs & Symptoms:

- The symptoms of RDS usually peak by the third day, and they may resolve quickly when diuresis starts and when infants begin to need less oxygen and mechanical ventilation.
  - The rapid fall in pulmonary vascular resistance and a rise in systemic arterial pressure sometimes leads to the development of a large left-to-right shunt through a PDA. Therefore, the patient's recovery may be interrupted by the development pulmonary edema.

Respiratory Distress Syndrome (RDS)

Treatment:

- Oxygen therapy
- Positive pressure/CPAP/Vapotherm
  - Adequate positive pressure to help prevent atelectasis
- Ventilation
  - Conventional ventilation
  - HFOV
- Surfactant – early dosing

Exogenous Surfactants

- Synthetic
  - Exosurf –
    - Does not contain proteins
    - No longer available
  - Surfaxin
    - Contains biologically active peptide to mimic action of SP-B
- Natural – derived from animal sources
  - Survanta® (beractant)– calf lung extract
  - Infasurf® (calfactant)– calf lung lavage
  - Curosurf® (poractant alpha)– pig lung extract

Note: Survanta & Curosurf in formulary at CNMC

Exogenous Surfactants

- Survanta or Curosurf can be given
- Patients admitted after being given one surfactant should be re-dosed with the same surfactant
- Advantages
  - Curosurf smaller dose
  - No clinical outcome advantage of one surfactant over the other

Exogenous Surfactants

- Dosing –
  - Start when patient is intubate with FIO_2 requirement >50 percent
  - Repeat doses given when FIO_2 is not reduced to less than 40% at dosing time interval
  - Dosing should be done with a Fellow/NNP/PA to assure proper technique

Respiratory Distress Syndrome (RDS)

Outcome:

- Infants not receiving assisted ventilation, clinical improvement is associated with the slow clearing of the lungs and a patchy return of normal alveolar aeration. No residual changes are observed, and postrecovery pulmonary function is normal.
- Infants who receive assisted ventilation, residual pulmonary changes are common and referred to as BPD (see BPD module)

Respiratory Distress Syndrome (RDS)

Mortality/Morbidity:

- RDS is a leading cause of mortality in infants and accounts for 20% of all neonatal deaths.
- Mortality rates have dramatically decreased in infants with RDS with the use of continuous positive-pressure ventilation with end-expiratory positive pressure and surfactant replacement therapy.
- Mortality rates associated with HMD are less than 10% for neonates older than 28 weeks' gestation.

Respiratory Distress Syndrome (RDS)

- Death often directly results from pulmonary disease.
  - However, it may also result from complications related to:
    - hypoxemia (e.g., intracranial hemorrhage
    - Sepsis/disseminated intravascular coagulation [DIC],
    - complications of assisted ventilation (e.g., pulmonary interstitial emphysema [PIE], pneumothorax, pneumomediastinum, gas embolism).