Pathophysiology

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Lecture 11

I. Disorders of Respiratory system

I. Pneumonias

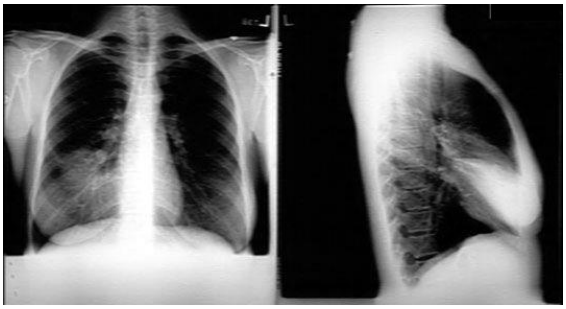
An acute inflammation of the lung parenchyma distal to the terminal bronchioles (consisting of the respiratory bronchiole, alveolar ducts, alveolar sacs and alveoli). Th e terms 'pneumonia' and 'pneumonitis' are often used synonymously for inflammation of the lungs, while 'consolidation' (meaning solidification) is the term used for gross and radiologic appearance of the lungs in pneumonia. It is caused by:

1- Infection, usually by bacteria, viral .
2- Foreign particle inhalation.
3- Irradiation.

Classification of Pneumonia

Based on the anatomical part of the lung parenchyma involved:

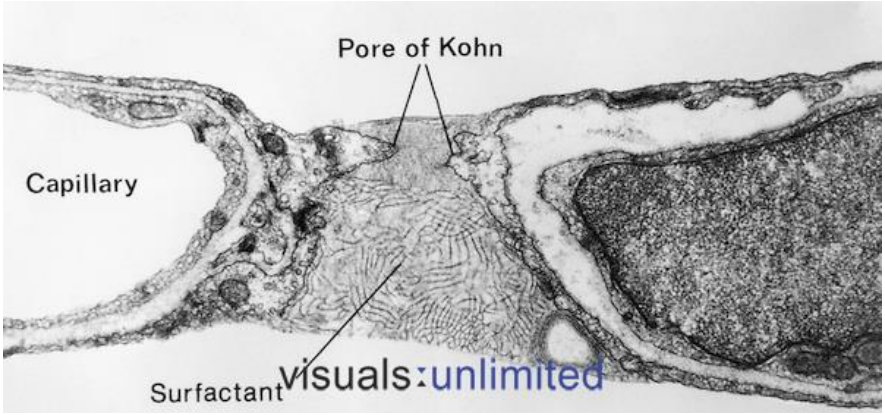
1- *Lobar pneumonia*:



Occurs due to **acute bacterial infection of part of a lobe or complete lobe.** Whole lobe is often affected as the inflammation spreads through the **pores of Kohn** (*also known as interalveolar connections) are discrete holes in walls of adjacent alveoli* and **Lambert channels (***are accessory connections in the lungs between some bronchioles and their adjacent alveoli***) .**

A- Commonly Streptococcus pneumoniae, Staphylococcus aureus, β Hemolytic streptococci and

B- less commonly Haemophilus influenzae, Klebsiella pneumoniae are responsible for lobar pneumonia.



2- *Bronchopneumonia (lobular)*:

Acute bacterial infection of the ***terminal bronchioles*** *characterized by purulent exudates which extends into surrounding alveoli through endobronchial route resulting into* ***patchy consolidation.*** It is usually seen in **extremes of age** and in association with chronic debilitating conditions. **Commonly** Streptococci, Staphylococcus aureus, β-Hemolytic streptococci, Haemophilus influenzae, Klebsiella pneumonia and Pseudomonas are responsible for Bronchopneumonia.

Bronchopneumonia (lobular) often leads to lobar pneumonia as the infection progresses. The same organism may cause one type of pneumonia in one patient, and another in a different patient.

3- ***Interstitial pneumonia***:

Patchy inflammatory changes, caused by **Viral or mycoplasma infection, mostly confined to the interstitial tissue of the lung without alveolar exudates.** It is characterized by **alveolar septal oedema and mononuclear infiltrates.** Commonly Mycoplasma pneumoniae, Respiratory syncytial virus, Influenza virus, adenoviruses, cytomegaloviruses and uncommonly Chlamydia and Coxiella are responsible for Interstitial pneumonia.

Age group	Predominant organisms**
0 to 1 months	Group B streptococcus Gram negative organisms *Chlamydia trachomatis* *Listeria monocytogenes*
1 to 24 months	Respiratory syncytial virus (RSV) and other viruses **(Influenza A and B, parainfluenzae 1-3 , adenoviruses, human)** *Streptococcus pneumoniae* *Haemophilus influenzae* (non typeable) *Bordetella pertussis*
2 to 5 years	Respiratory syncytial viruses (RSV) and other viruses **(Influenza A and B, parainfluenzae 1-3 , adenoviruses, human)** *Streptococcus pneumoniae* *Haemophilus influenzae* (non typeable)
6 to 18 years	*Mycoplasma pneumoniae* *Chlamydia pneumoniae* *Streptococcus pneumoniae* accounts for up to 30% Respiratory viruses account for < 15% of episodes

** ***Staphylococcus aureus is an important pathogen of serious pneumonia to remember in all age groups.***

Mode of transmission

1. ***Inhalation*** of the microbes present in the air.
2. ***Aspiration*** of organisms from the nasopharynx or oropharynx.
3. ***Hematogenous spread*** from a distant focus of infection.
4. ***Direct spread*** from an adjoining site of infection.

Pathophysiology

The normal lung is free of bacteria because of the presence of a number of lung defense mechanisms at different levels such as:

1. **Nasopharyngeal filtering action**,
2. **Mucociliary action** of the lower respiratory airways,
3. The presence of **phagocytosing alveolar macrophages.**
4. **Immunoglobulins**. Failure of these defense mechanisms and presence of certain predisposing factors result in pneumonias.

These conditions are as under:

1. **Altered consciousness:** The oropharyngeal contents may be aspirated in states causing unconsciousness e.g. in coma, cranial trauma, seizures, cerebrovascular accidents, drug overdose, alcoholism etc.

2. **Depressed cough and glottis reflexes**: Depression of effective cough may allow aspiration of gastric contents e.g. in old age.
3. **Impaired mucociliary transport.**
4. **Impaired alveolar macrophage function**: Pneumonias may occur when alveolar macrophage function is impaired e.g. by cigarette smoke
5. **Endobronchial obstruction**, e.g. chronic bronchitis.
6. **Immunocompromised states**, e.g. AIDS.

Any immunogenic agent that reaches the alveoli lead to inflammation reaction against it.

A. WBCs migrates to alveoli space.
B. The alveoli become more thick due to the reaction against that specific immunogen.
C. Pneumonia passes into **<u>four stages</u>**:

1- **Stage of congestion**:

a) This stage represents **early acute inflammatory response**.
b) Affected lobe becomes **red and heavy due to vascular congestion**.
c) Copious proteinaceous fluid, abundant neutrophils and many bacteria can be seen in the alveoli.
d) This stage **lasts for 1 to 2 days**.

2- **Stage of red hepatisation**:

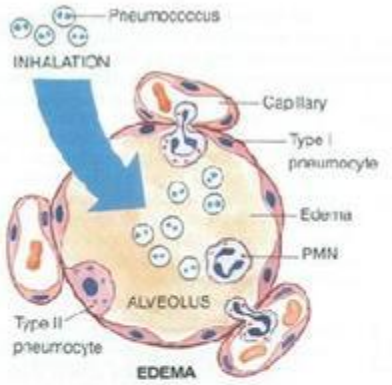
a) Affected lobe becomes **red**.
b) Firm and acquires liver like consistency.
c) Proteinaceous fluid transforms into fibrin strands with marked cellular exudates of neutrophils.
d) Extravasation of red cells which give red color to consolidated lung.
e) This stage **lasts for 2 to 4 days**.

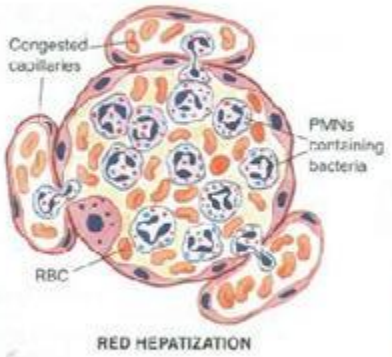
3- **Stage of gray hepatisation**:

a) Affected lobe becomes dry, firm.
b) Gray due to lysed red cells.
c) Neutrophilic cellular exudates decreases due to breakdown of inflammatory cells.
d) Macrophages are now seen.
e) Microorganism load also reduces.
f) This stage **lasts for 4 to 7 days**.

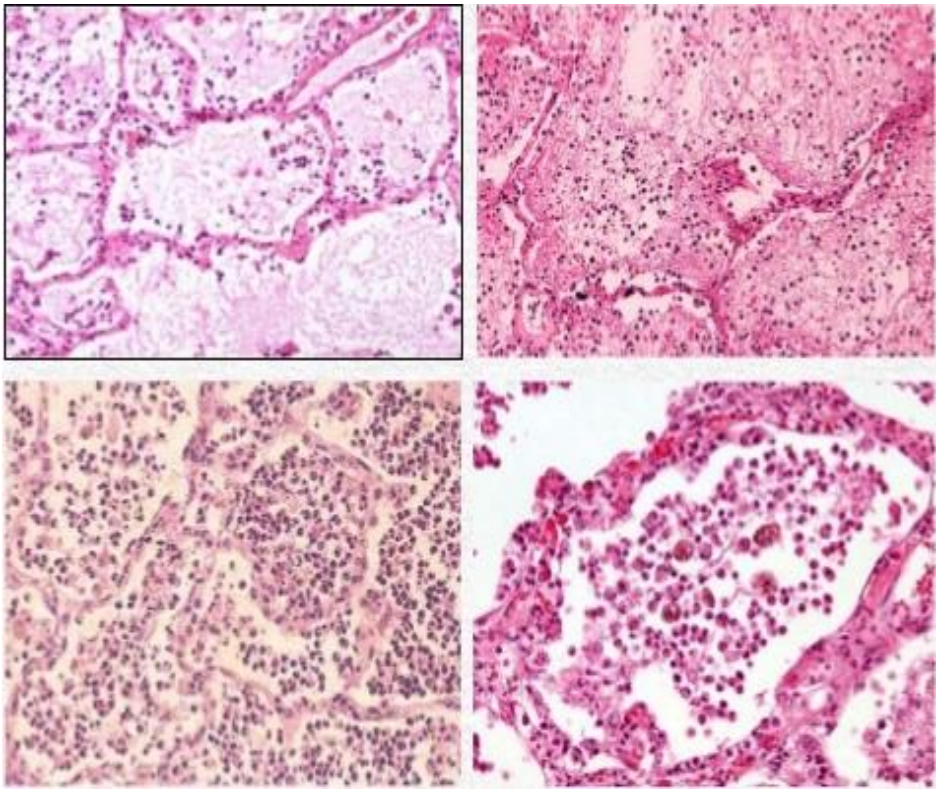
4- **Stage of resolution:**

a) Due to **enzymatic action**, fibrinous matter is **liquefied**.
b) The lung **aeration is re-establish** gradually.
c) **Macrophages are the major cells** in the alveoli.
d) There is progressive **reduction of fluid and cellular exudates** from the alveoli by way of expectoration and lymphatic drainage.
e) Leading to **normal lung** parenchyma in **over 3 weeks**.
f) The involved areas by inflammation are **not adequately ventilated**, due to secretion and edema.
g) This will lead to **partial occlusion of alveoli** and bronchi causing a decrease in alveolar oxygen content.


Pneumococcus
INHALATION
Capillary
Type I pneumocyte
Edema
PMN
ALVEOLUS
Type II pneumocyte
EDEMA


Congested capillaries
PMNs containing bacteria
RBC
RED HEPATIZATION

Fibrin
Macrophage
GREY HEPATIZATION



II. Tuberculosis

Tuberculosis, commonly known as TB, is a contagious and an often severe airborne disease caused by a bacterial infection.
TB typically affects the lungs, but it also may affect any other organ of the body.

Factors that influence the likelihood of transmission

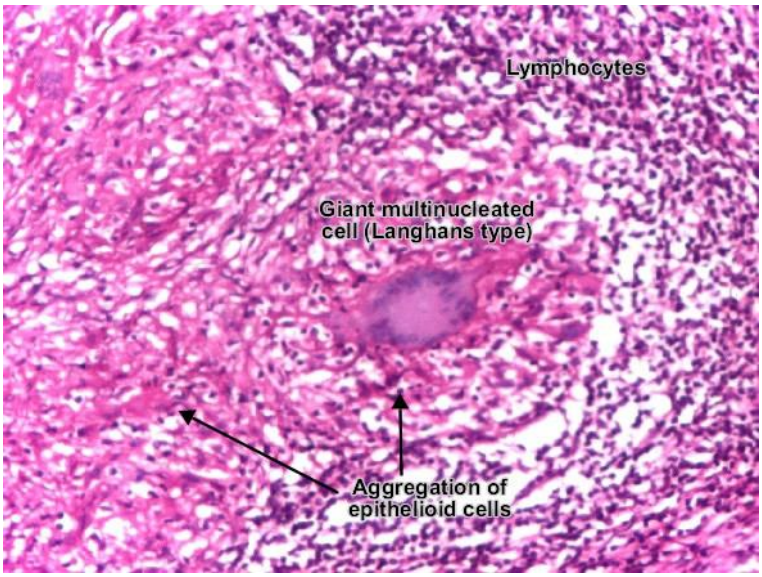
1. **Number of organisms** expelled into air.
2. **Concentration of organisms**.
3. **Length of time of exposure**.
4. **Immune system** of the exposed person.

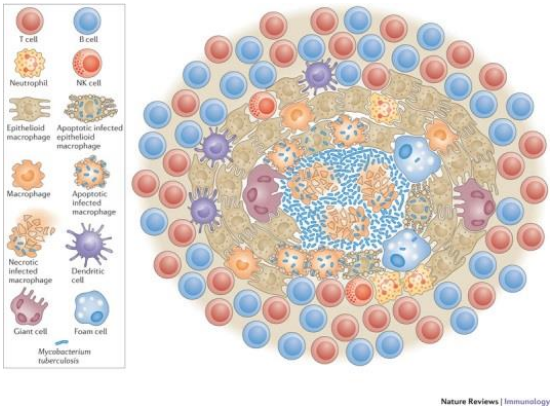
TB: Pathophysiology

Mycobacterium Tuberculosis is acid-fast, aerobic bacilli. Lipid-rich cell wall, making the organism resistant to disinfectants, detergents, common antibacterial antibiotics and traditional strains.

a) The bacteria is capable of **intracellular growth** in **inactivated alveolar macrophage**.
b) The rout of transmission is mainly **by airborne droplets** through talking and coughing.
c) **A brief exposure to tubercle bacilli rarely causes infection**.
d) TB is not usually highly infectious, transmission requires frequent, **close, or prolonged exposure.**
e) When inhaled; they are lodged into the bronchioles and alveolus.
f) M. tuberculosis **replicates slowly** over time.
g) It travels through lymphatic system to find a suitable environment for growth
h) **Primarily in the: Upper lobes of the lungs**, but also the Kidneys, Epiphyses of the bones, Cerebral cortex and Adrenal glands.
i) Infection occurs when a person inhales droplet nuclei containing tubercle bacilli that reach the alveoli of the lungs.
j) These tubercle bacilli are **ingested by alveolar macrophages**;
k) Since these macrophages are unable to destroy the bacteria the inflammatory response will become a **chronic granulomatous inflammation** **which is characterized by:**

1- **Epithelioid cells** :— *Macrophages that have undergone a specialized transformation to have tightly interdigitated cell membranes that link adjacent cells.* Epithelioid cells can **be highly phagocytic.**
2- Granuloma macrophages can also fuse into **multinucleated giant cells**.
3- **Foam cells**:- *Macrophage characterized by lipid accumulation most frequently located at the rim of the necrotic center of a mature tuberculous granuloma*.





4- Bacteria are most commonly present in the **central necrotic areas** in which dead and dying macrophages can be seen. (**caseation necrosis**)
5- Many other cell types also populate the granuloma, such as **dendritic cells**, **B and T cells**, **natural killer** (NK) cells, **fibroblasts** and cells that secrete extracellular matrix components.

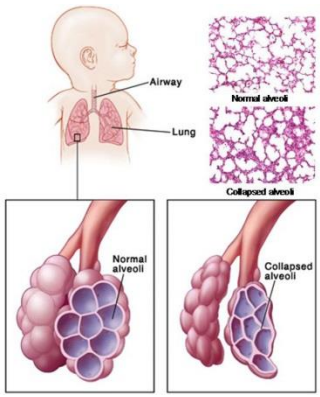
1. The **majority** of these bacilli are **destroyed or inhibited**.
2. A small number **may multiply intracellularly** and are released when the macrophages die.
3. If alive, these bacilli may spread by way of lymphatic channels **or** through the bloodstream to more distant tissues and organs (including areas of the body in which TB disease is most likely to develop: regional lymph nodes, apex of the lung, kidneys, brain, and bone).
4. This process of dissemination primes the immune system for a systemic response.
5. Persons with **Latent Tuberculosis Infection** (LTBI) have M. tuberculosis in their bodies, **but do not have TB disease and cannot spread the infection to other people.**
    a) A person with LTBI is not regarded as having a case of TB.
    b) The process of LTBI begins when extracellular bacilli are ingested by macrophages and presented to other white blood cells.
    c) This triggers the immune response in which white blood cells kill or encapsulate most of the bacilli, leading to the formation of a granuloma.
    d) At this point, LTBI has been established.
    e) LTBI may be detected by using the **tuberculin skin test (TST).**
    f) It can take **2 to 8 weeks after the initial TB infection** for the body's immune system to be able to react to tuberculin and for the infection to be detected by the TST.
    g) Within weeks after infection, the immune system is usually able to halt the multiplication of the tubercle bacilli, preventing further progression.

6. The tubercle bacilli overcome the immune system and multiply, resulting in progression from LTBI to TB disease.
7. Persons who have TB disease are usually infectious and **may spread the bacteria to other people.**
8. The progression from LTBI to TB disease may occur at any time, from soon to many years later.
9. Body fluid or tissue from the disease site should be collected for AFB smear and culture. Positive culture for M. tuberculosis confirms the diagnosis of TB disease.

	Person with LTBI (Infected)	**Person with TB Disease (Infectious)**
1	Has a small amount of TB bacteria in his/her body that are alive, but inactive	Has a large amount of active TB bacteria in his/her body
2	**Cannot** spread TB bacteria to others	May spread TB bacteria to others
3	Does **not** feel sick, but may become sick if the bacteria become active in his/her body	May feel sick and may have symptoms such as a cough, fever, and/or weight loss
4	Usually has a TB skin test or TB blood test reaction indicating TB infection	Usually has a TB skin test or TB blood test reaction indicating TB infection
5	Radiograph is typically **normal**	Radiograph may be **abnormal**
6	Sputum smears and cultures are **negative**	Sputum smears and cultures may be **positive**
7	Should treatment for LTBI to prevent TB dis.	Needs treatment for TB disease
8	Does **not** require respiratory **isolation**	May require respiratory isolation
9	**Not** a TB case	A TB case

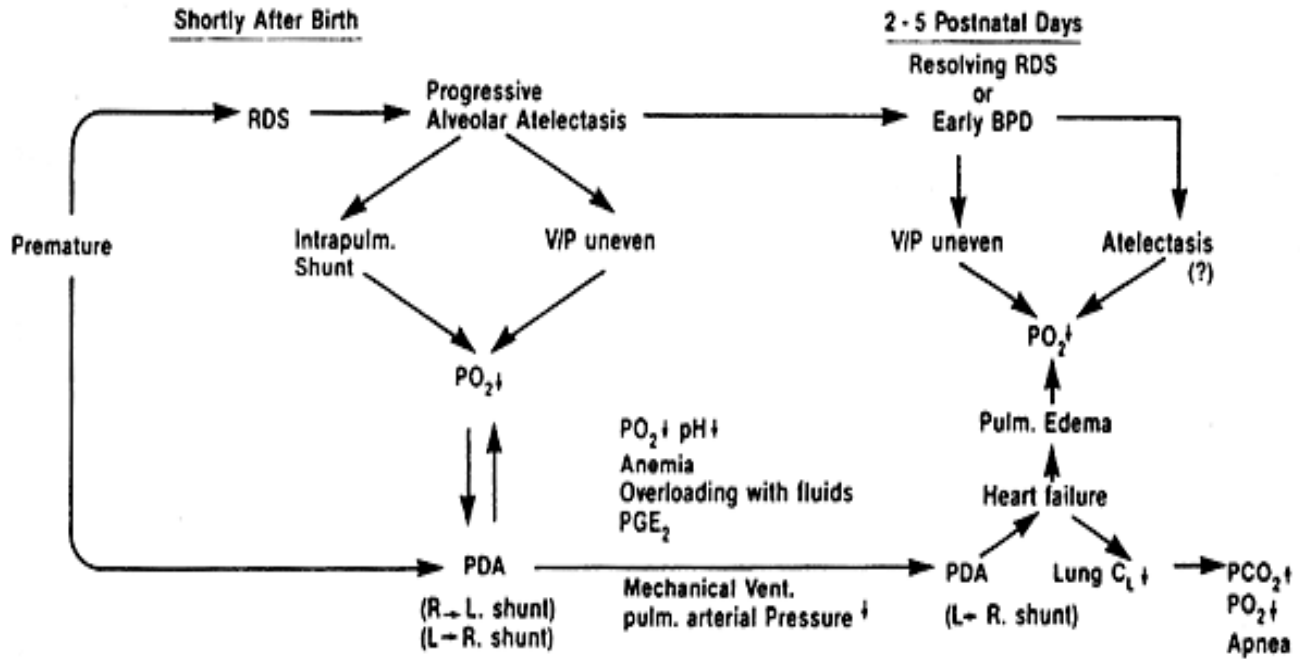
III. Respiratory Distress Syndrome —abbreviation (*RDS*)

respiratory disorder that occurs in newborn premature infants and is characterized by deficiency of the surfactant coating the inner surface of the lungs, by failure of the lungs to expand and contract properly during breathing with resulting collapse, and by the accumulation of a protein-containing film lining the alveoli and their ducts; called also ***hyaline membrane disease***. RDS almost always occurs in newborns born **before 37 weeks of gestation.** The more premature the baby is, the greater is the chance of developing RDS.



Surfactant, A mixture of **phospholipids and lipoproteins**, is secreted by lung cells.

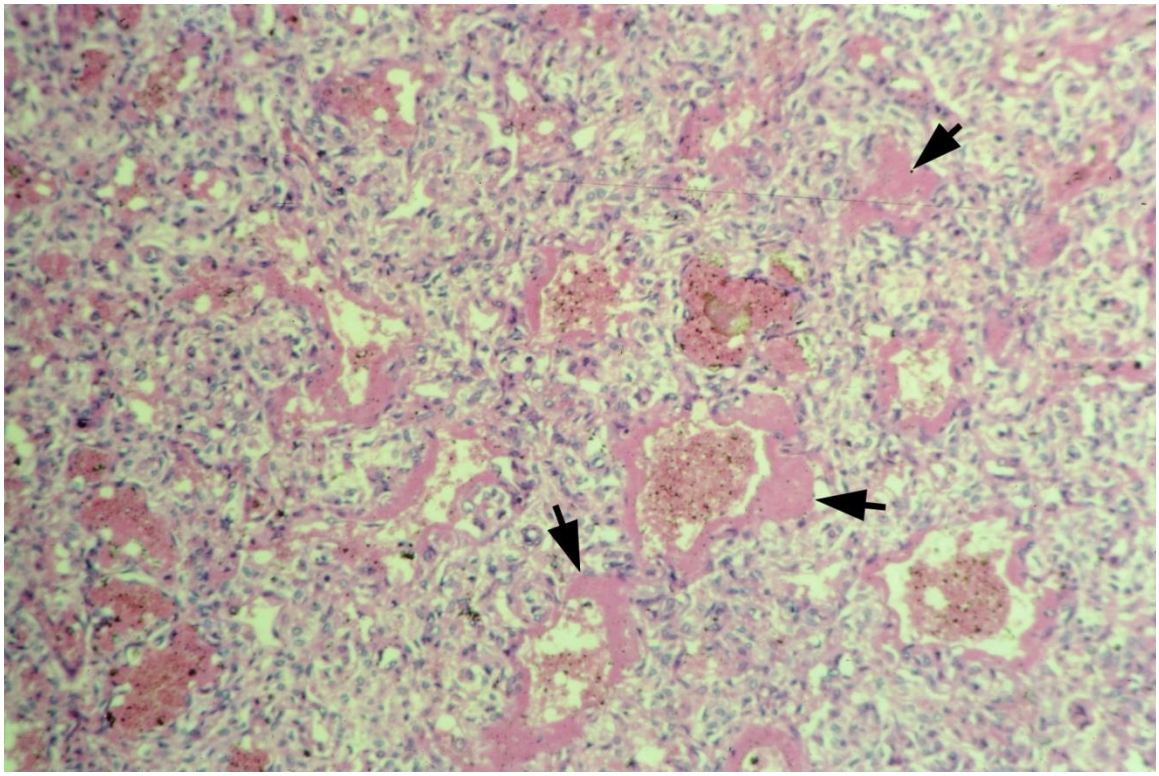
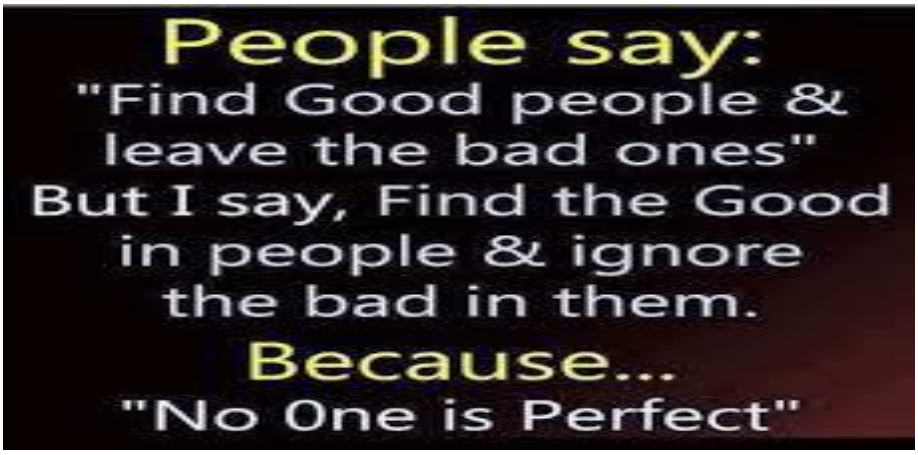
PATHOPHYSIOLOGY:



1. The primary cause of RDS is **inadequate pulmonary surfactant**.
2. The structurally immature and surfactant-deficient lung has decrease ↓ **compliance** and a **tendency to atelectasis**;
3. Other factors **in preterm infants** that increase ↑ the risk of atelectasis are **decreased alveolar radius and weak chest wall**.
4. With atelectasis, well perfused but poorly ventilated areas of lung lead to V/Q mismatch ***the ventilation/perfusion ratio*** (with intra-pulmonary shunting).
5. Alveolar hypoventilation will result in **hypoxemia and hypercapnia**.
6. **Severe hypoxemia and systemic hypoperfusion** result in decreased O2 delivery, anaerobic metabolism and subsequent **lactic acidosis**.
7. **Hypoxemia and acidosis** may further **impair oxygenation** by causing **pulmonary vasoconstriction**, resulting in **right-to-left shunting** at the levels of the foramen ovale and ductus arteriosus.
8. Other factors, such as baro/volutrauma (***damage to the lung caused by overdistension***) and high FIO_2 (***fraction of inspired air***), may initiate release of inflammatory cytokines and chemokines causing more **endothelial and epithelial cell injury**.

9. The injury results in reduced surfactant synthesis and function as well as **increased endothelial permeability leading to pulmonary edema**.
10. Leakage of proteins into the alveolar space further exacerbates surfactant deficiency by causing surfactant inactivation.

Macroscopically, the lungs appear **congested, atelectatic and solid**.

Microscopically:

a) Diffuse **alveolar atelectasis**.
b) Pulmonary **edema** are seen.
c) An **eosinophilic membrane** composed of a fibrinous matrix of materials from the blood and cellular debris (**the hyaline membrane**) lines the visible airspaces that usually constitute dilated terminal bronchioles and alveolar ducts.