Diseases of the respiratory system

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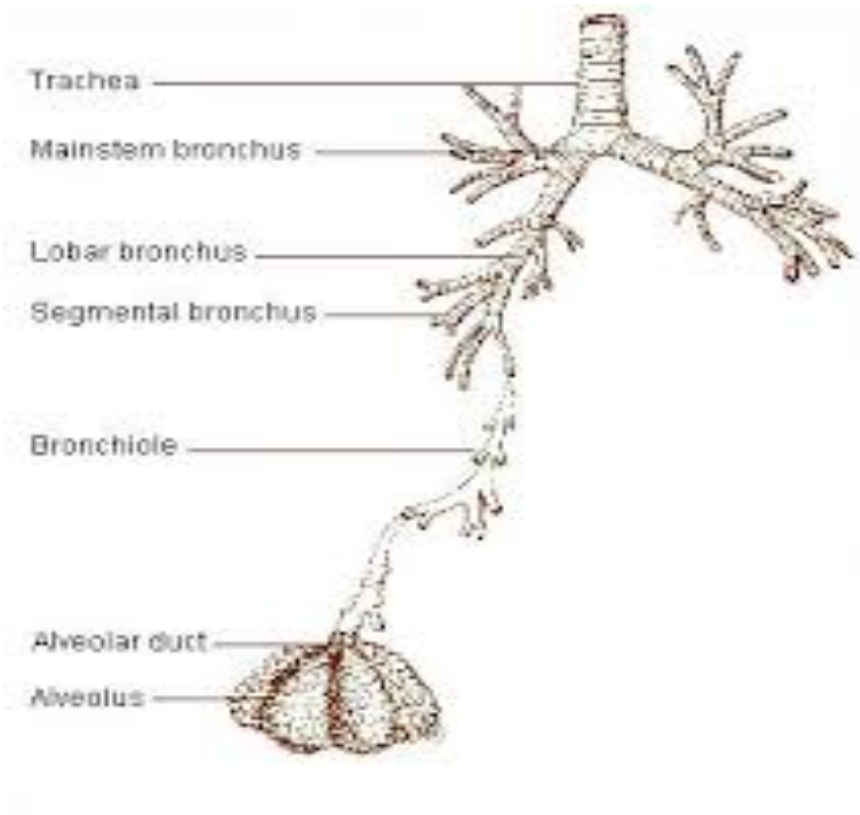
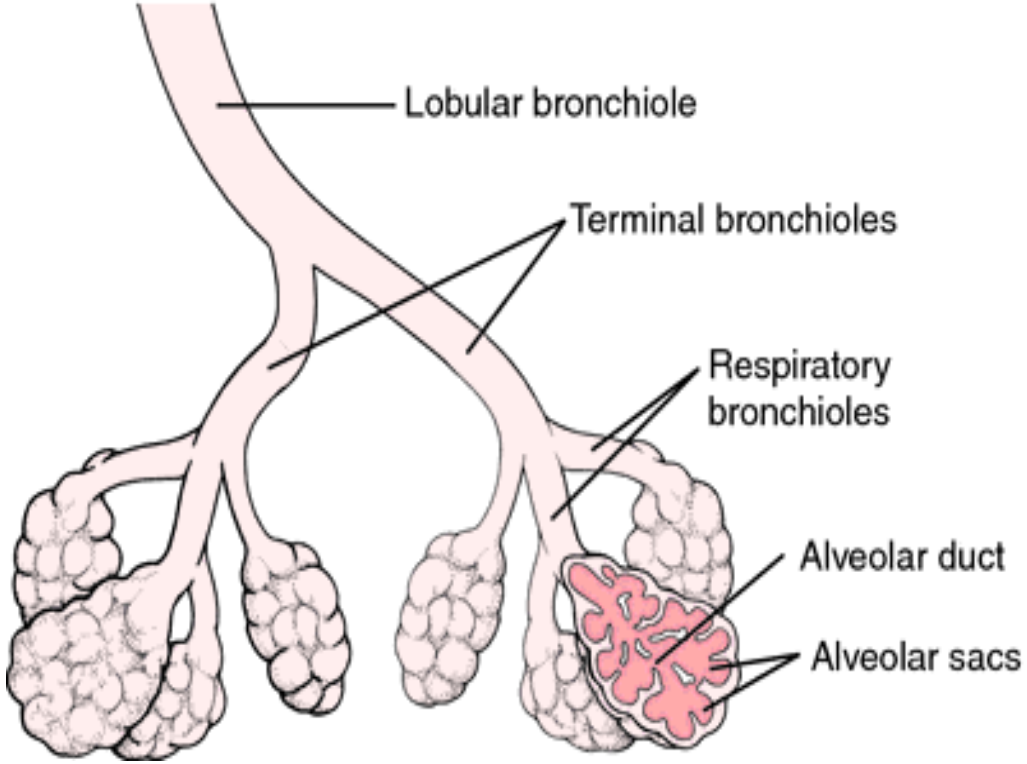
FRCPath

STRUCTURE OF THE RESPIRATORY SYSTEM



The part of the lung distal to terminal bronchioles= acinus
note: every 3-5 acini form a lobule.



alveoli

- Alveoli are the site of gas exchange
- Alveoli are lined by flat pneumocytes (type I pneumocytes that occupy 95% of the alveolar surface) and type II pneumocytes .
- type II pneumocytes secrete **surfactant** and are the main cells involved in **repair** after injury of type I pneumocytes.

- **Surfactant lowers the surface tension inside the alveolar membrane to prevent them from collapsing during exhalation..**
- Surfactant in the lung is important so the alveoli do not collapse after expiration.

Diffusion of gases

- Oxygen and CO2 exchange happens through diffusion
- Diffusion depends on: surface area, thickness of the diffusion membrane and concentration gradient.. All criteria favoring maximum diffusion are seen in the alveoli.

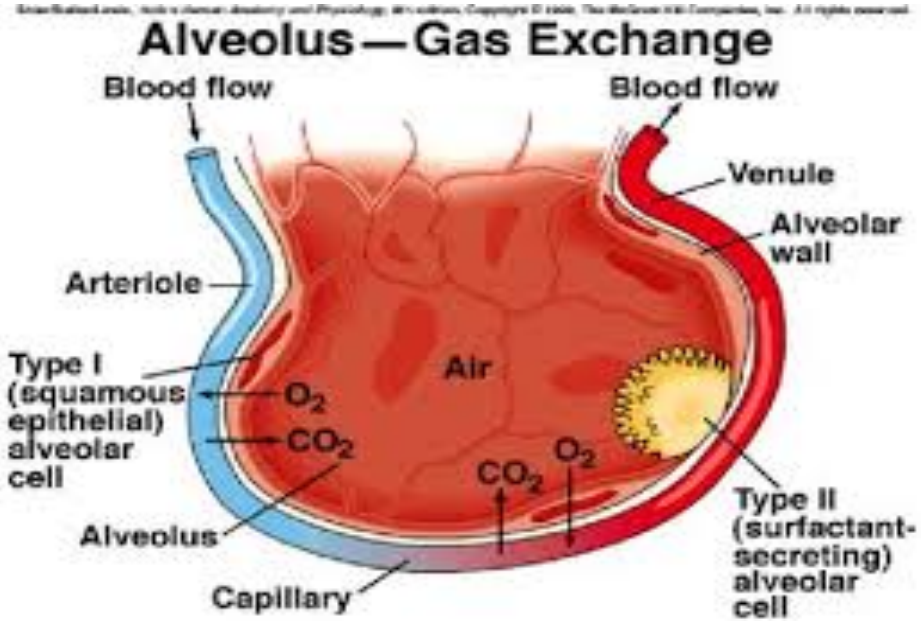
Alveoli are designed to achieve maximum gas exchange :

1.They have a huge surface area

2.Thin diffusion membrane

3.Concentration gradient kept to maximum because of the rich blood supply

ALVEOLI


Alveolus—Gas Exchange
Blood flow
Blood flow
Venule
Alveolar wall
Arteriole
Type I (squamous epithelial) alveolar cell
Air
O_2
CO_2
CO_2
O_2
Alveolus
Capillary
Type II (surfactant-secreting) alveolar cell

ALVEOLI: LARGE SURFACE AREA

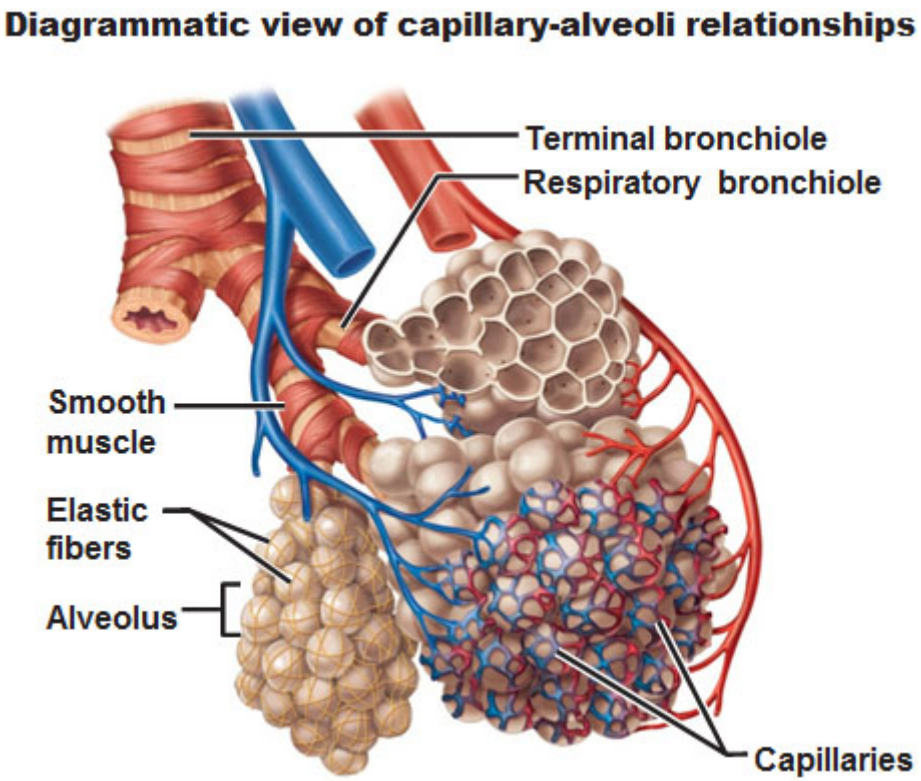
Lungs

A pair of lungs contains about ***300 million alveoli.***

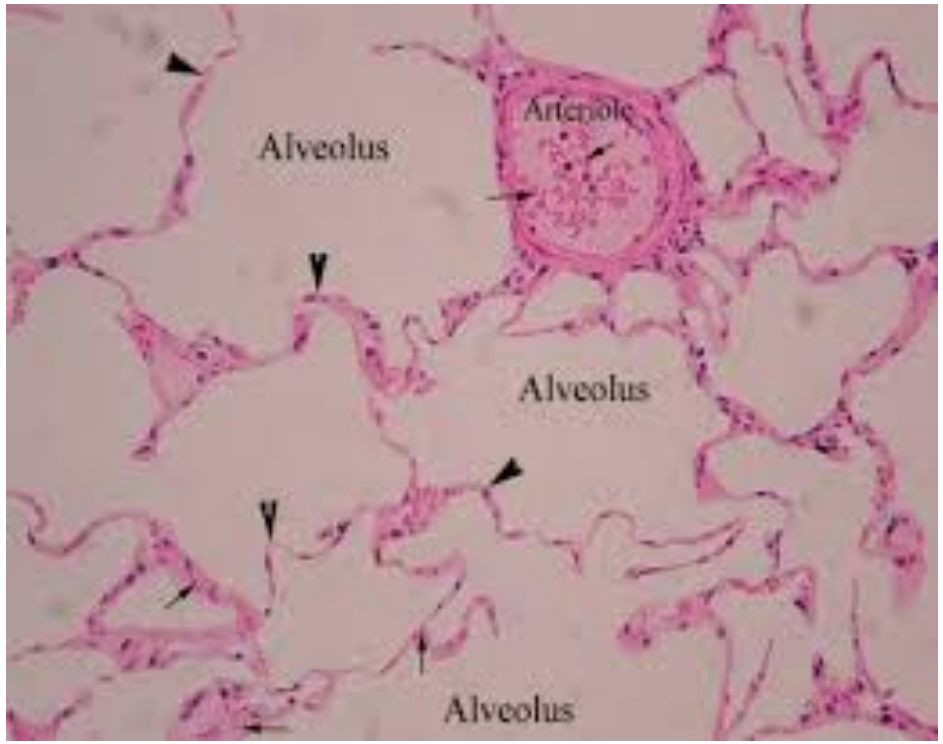
This subdivides the volume of the lungs and creates a total alveolar surface area of about 1000 ft.^{2} (like a room 33 ft. x 30 ft.).

The advantage to having this is that it allows for a very ***large surface area for gas exchange.***

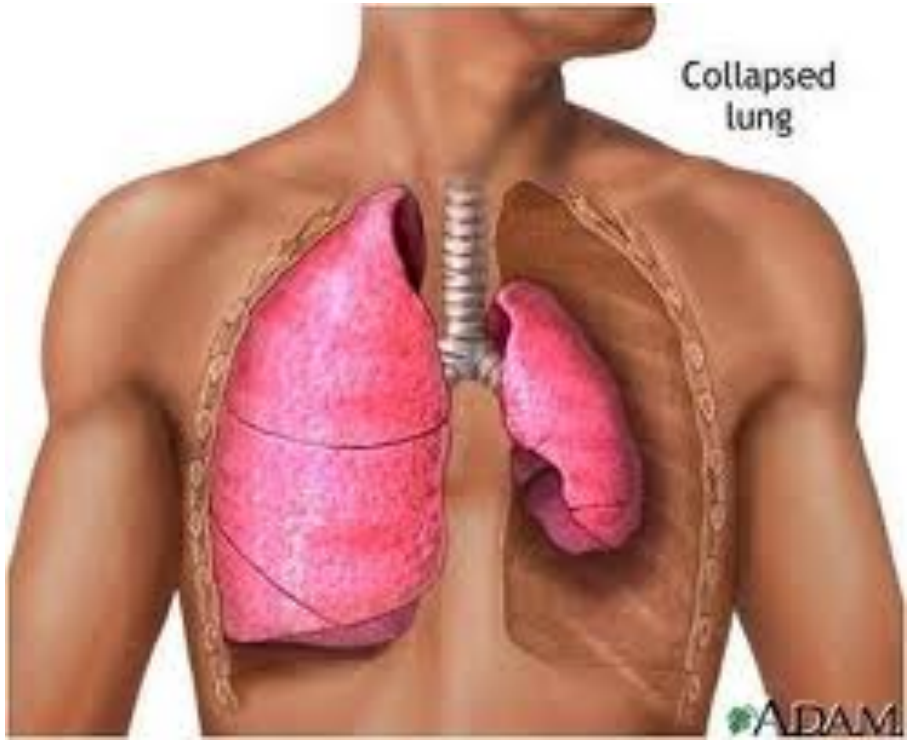
ALVEOLI: RICH BLOOD SUPPLY which keeps a high concentration gradient



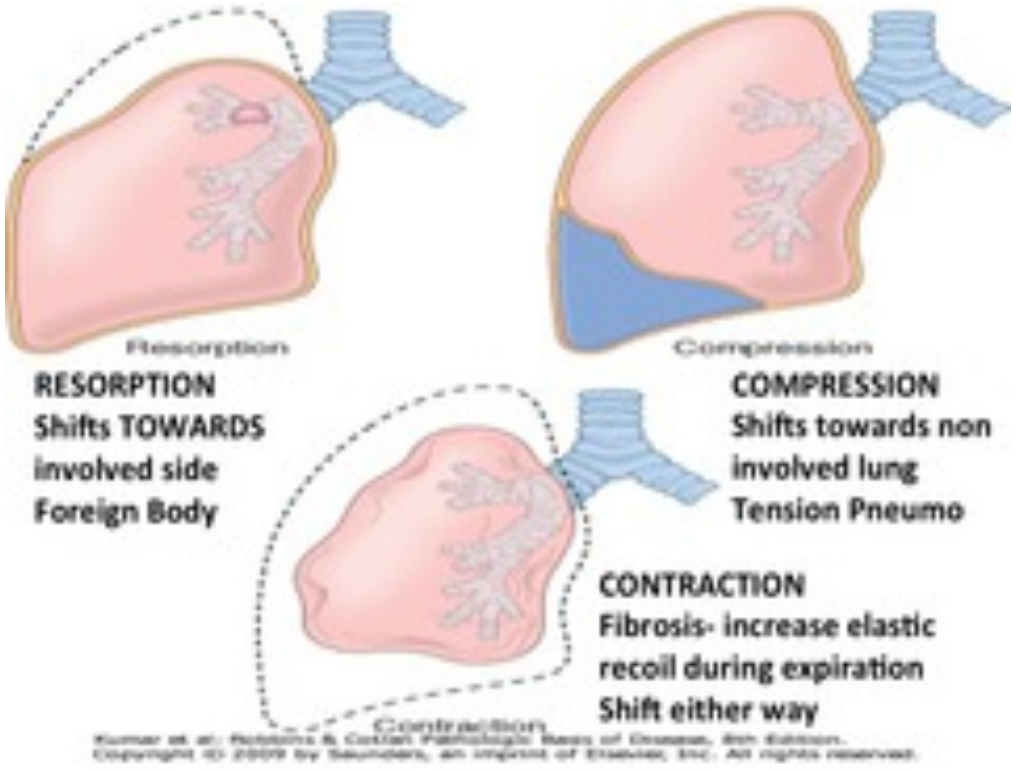
ALVEOLI: THIN MEMBRANES



ATELECTASIS = LUNG COLLAPSE =انْخِماص



TYPES OF ATELECTASIS



RESORPTION ATELECTASIS

- ***OBSTRUCTION BY:***

  *MUCOUS OR MUCOPURULENT PLUG (POST-OP, ASTHMA, BRONCHIECTASIS OR CHRONIC BRONCHITIS)

  *TUMOUR.

  *FOEIGN BODY .

COMPRESSION ATELECTASIS

ACCUMOLATION OF :

- *FLUID* (PLEURAL EFFUSION)
- BLOOD (HAEMOTHORAX)
- AIR (PNEUMOTHORAX)

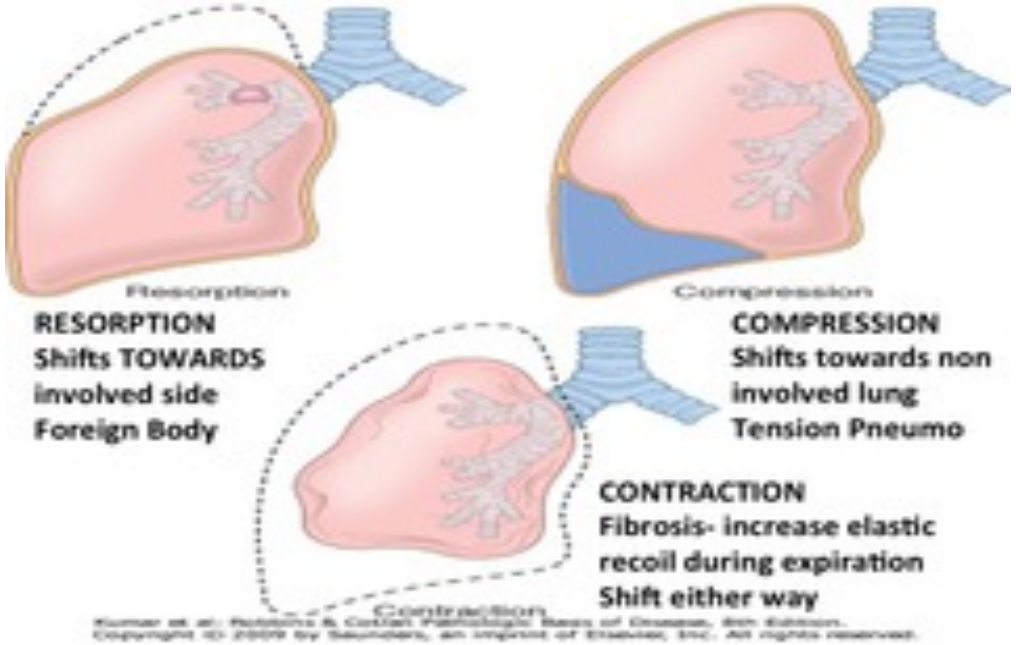
ALL WITHIN THE PLEURAL CAVITY.

- Compression can also be due to elevated diaphragm
- This occurs post-op and due to ascitis

CONTRACTION ATELECTASIS

- LOCAL OR GENERALISED FIBROSIS.

- ATELECTASIS…….IS IT REVERSIBLE???????



Atelectasis (except when caused by contraction) is potentially reversible and should be treated promptly to prevent hypoxemia and superimposed infection of the collapsed lung.

Question: what are the complications of atelectasis? ……. Answer: Read above

Acute lung injury and ARDS (adult respiratory distress syndrome)

- **متلازمة الضائقة التنفسية الحادة = ARDS**

- Acute lung injury includes a spectrum of bilateral pulmonary damage (endothelial and epithelial), which can be initiated by numerous conditions.

Acute lung injury manifests as:

1. Acute onset of dyspnea,
2. Decreased arterial oxygen pressure (hypoxemia),refractory to oxygen
3. Development of bilateral pulmonary infiltrates on the chest radiograph (due to pulmonary edema)
4. Absence of clinical evidence of primary left-sided heart failure

NOTE:

The pulmonary infiltrates in acute lung injury are caused by damage to the alveolar capillary membrane, rather than by left-sided heart failure , such accumulations constitute an example of *noncardiogenic pulmonary edema*.

- **<u>Note</u>**-
- Acute lung injury can progress to the more severe *acute respiratory distress syndrome*

ARDS

- clinical syndrome caused by diffuse, bilateral alveolar capillary and epithelial damage.

The usual course is characterized by:

A. Rapid onset of life-threatening respiratory insufficiency

B. severe arterial hypoxemia that is refractory to oxygen therapy and may progress to multisystem organ failure

ARDS

- Occurs in a multitude of clinical settings
- And is associated with either

a. Direct injury to the lung or

b. Indirect injury in the setting of a systemic process

Direct Lung Injury

I. Common Causes

1. Pneumonia
2. Aspiration of gastric contents

II. Uncommon Causes

1. Pulmonary contusion

- Indirect causes

I. common causes

1. Sepsis

2. Severe trauma with shock

II. Uncommon causes

Acute pancreatitis

Causes of ARDS

Direct lung injury	Indirect lung injury
Common causes: - Pneumonia - Aspiration of gastric contents	Common causes: - Sepsis - Severe trauma with shock and multiple transfusions
Less common causes: - Pulmonary contusion - Fat emboli - Near-drowning - Inhalational injury - Reperfusion pulmonary oedema	Less common causes: - Cardiopulmonary by-pass - Drug overdoes - Acute pancreatitis - Transfusion of blood products

Note:

- Respiratory distress syndrome of the newborn is pathogenetically distinct; it is caused by a primary deficiency of surfactant

PATHOGENESIS

- The alveolar-capillary membrane is formed by two separate barriers: the microvascular endothelium and the alveolar epithelium.
- In ARDS, the integrity of this barrier is compromised by either endothelial or epithelial injury, or, more commonly, both.

The acute consequences of damage to the alveolar capillary membrane include:

1. Increased vascular permeability and alveolar flooding
2. Loss of diffusion capacity,
3. Widespread surfactant abnormalities caused by damage to type II pneumocytes

Suggested mechanism:

- *In ARDS,* ***lung injury is caused by an imbalance of pro-inflammatory and anti-inflammatory mediators.***

ARDS: pathogenesis

A. Increased synthesis of interleukin 8 (IL-8), a potent neutrophil chemotactic and activating agent, by pulmonary macrophages. This is seen as early as the first 30 minutes of lung injury.

- B. Release of IL-1 and tumor necrosis factor (TNF), leading to endothelial activation

C. Activated neutrophils release a variety of oxidants, proteases, leukotrienes that cause damage to the alveolar epithelium and endothelium.

D- Combined assault on the endothelium and epithelium increases vascular leakiness and loss of surfactant that render the alveolar unit unable to expand.

- The destructive forces by neutrophils can be counteracted by
- 1. antiproteases
- 2.antioxidants
- 3. anti-inflammatory cytokines (**e.g., IL-10)**

- In the end, it is the balance between the destructive and protective factors that determines the degree of tissue injury and clinical severity of ARDS

Note:

- Neutrophils are thought to have an important role in the pathogenesis of ARDS

MORPHOLOGY

In the **acute phase of ARDS**

Gross,

1. The lungs are red, firm
2. Airless, and heavy.

Histopathological features of ARDS

1. Capillary congestion,
2. Necrosis of alveolar epithelial cells,
3. Interstitial and intra-alveolar edema and hemorrhage,
4. Increased numbers of neutrophils within the vascular space, the interstitium, and the alveoli
5. The most characteristic finding is the presence of **hyaline membranes** lining the alveolar ducts

Hyaline membrane

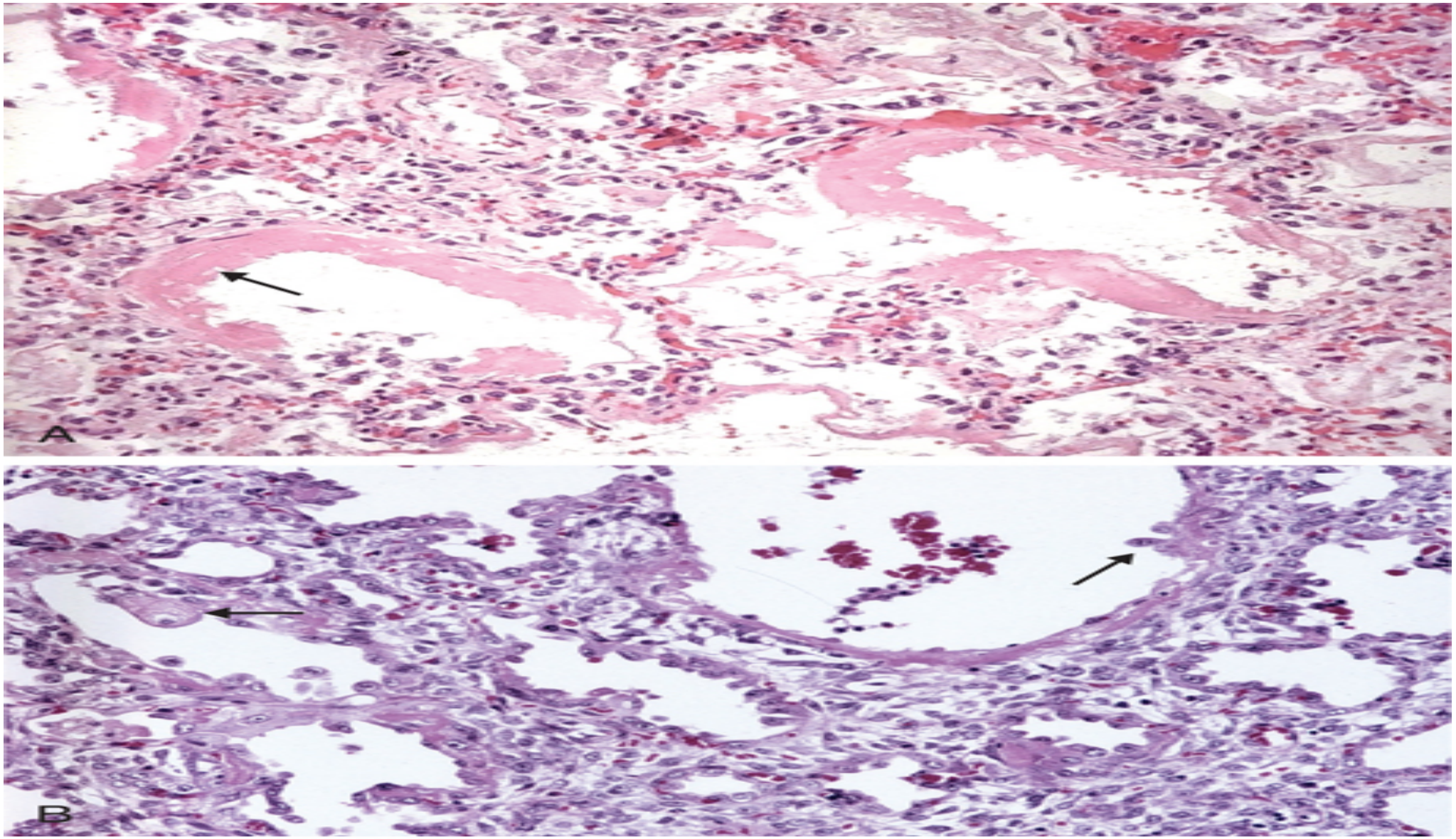
Composed of :

a. fibrin-rich edema fluid

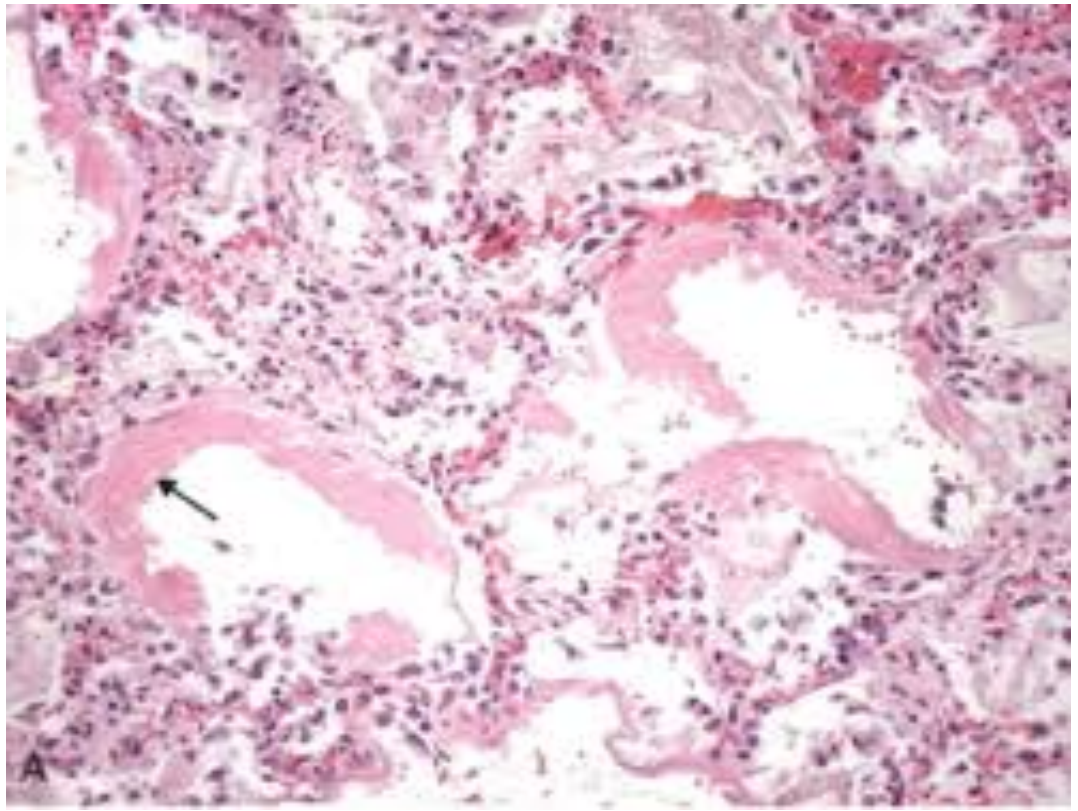
b. Remnants of necrotic epithelial cells.

NOTE: Overall, the picture is similar to that seen in respiratory distress syndrome in the newborn

ARDS



ARDS



Histological changes of ARDS

In the organizing stage,

- Vigorous proliferation of *type II pneumocytes* occurs in an attempt to regenerate the alveolar lining.

Histological changes after recovery

Resolution is unusual-

a. More commonly, there is *organization of the fibrin* exudates, with resultant *intra-alveolar fibrosis.*

b. Marked thickening of the alveolar septa occurs, caused by proliferation of interstitial cells and deposition of collagen..

ARDS: outcome

-With improvements in supportive therapy, the mortality rate ARDS cases occurring yearly has decreased from 60% to 40% in the last decade.

- If the patient survives the acute stage, diffuse interstitial fibrosis may occur, with continued compromise of respiratory function.
- in most patients who survive the acute insult and are spared the chronic fibrosis, normal respiratory function returns within 6 to 12 months

Predictors of poor prognosis include

- Advanced age
- Underlying bacteremia (sepsis)
- The development of multisystem (especially cardiac, renal, or hepatic) failure.

ARDS treatment (this is extra, just FYI)

- Supportive
- Teat in the ICU
- Intubation
- Give oxygen but avoid barotrauma!
- ECMO **(Extracorporeal membrane oxygenation**)