RS

PATHOLOGY

MODIFIED NO. ?

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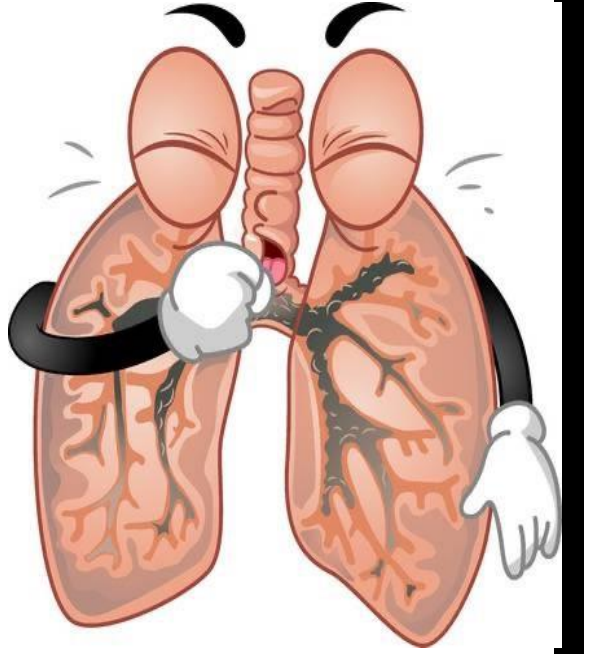

THE RESPIRATORY SYSTEM

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https://www.123rf.com/photo_38644498_stock-illustration-mascot-illustration-of-the-lungs-coughing-violently.html

Our lecture today includes 4 topics:

1) General Anatomical information

2) Atelectasis (lung collapse)

3) Acute Respiratory Distress Syndrome (ARDS)

4) Diffuse Pulmonary Diseases (obstructive vs restrictive)

Say بسم الله and start 

Topic 1

General Anatomical Information

The major function of the lung is to replenish oxygen and remove carbon dioxide from blood, meaning " Gases Exchange process".

The structure of tracheobronchial tree is perfectly created to fit this function. At the midline we have the trachea, which bifurcates at the level of the sternal angle into right & left main bronchi, then they undergo further division into a smaller respiratory passages, then each lobar bronchi (secondary bronchi) correlates with one lung lobe, then the segmental bronchi, then into the bronchioles which are distinguished from bronchi by the absence of cartilages and submucosal glands, and finally the terminal bronchiole.

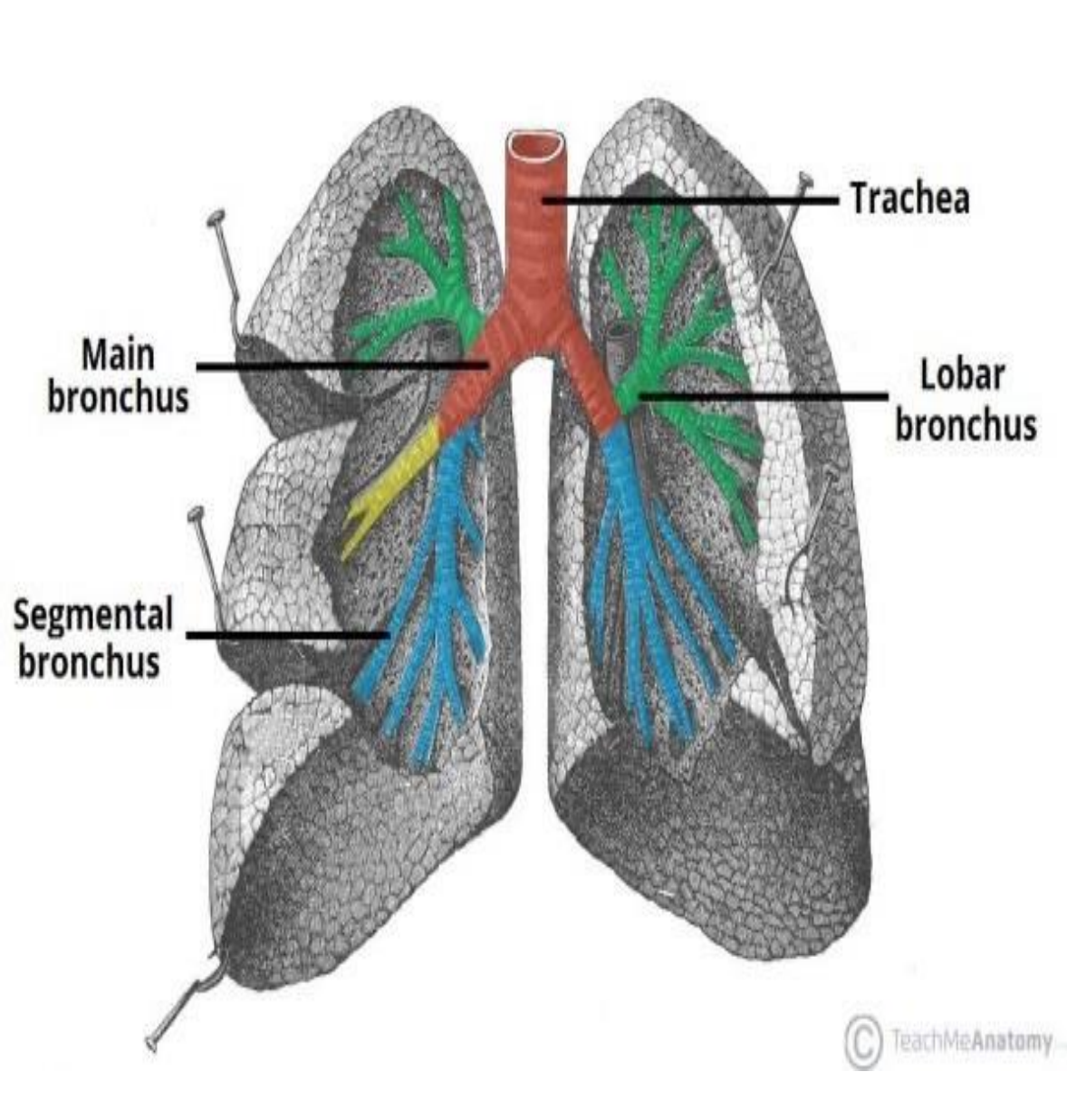
Distal to the terminal bronchioles we have acini which are:
1)the blind end of the respiratory passages
2) the ultimate point of gas exchange
3) the fundamental unit of the lung

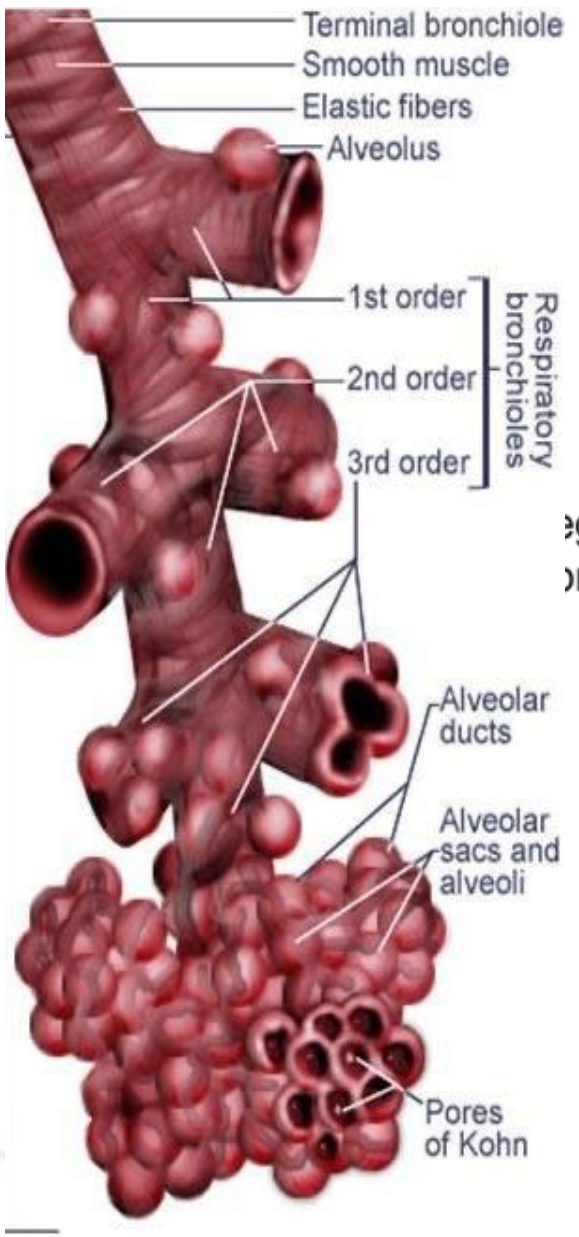
The acinus is made of [respiratory bronchioles (direct branches of terminal bronchioles) + alveolar ducts + alveolar sacs], and here where the gases exchange takes place.

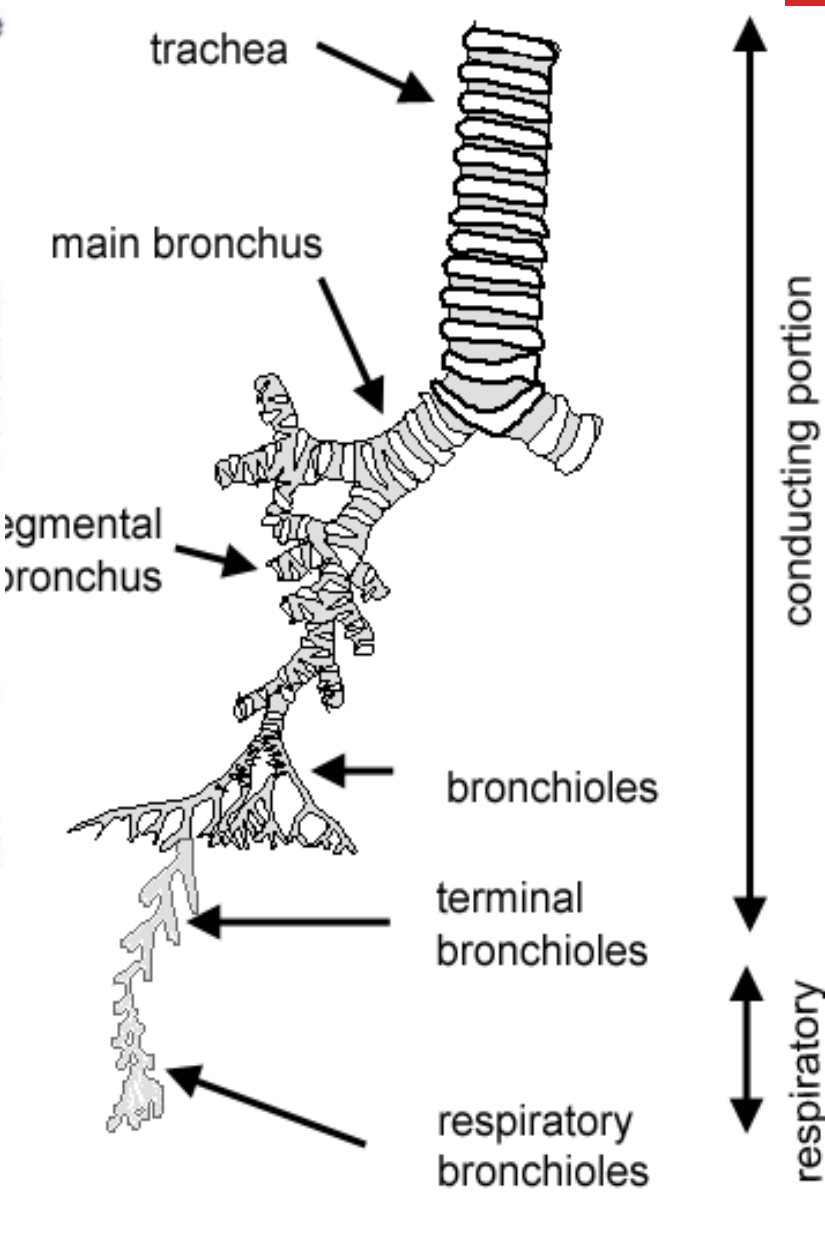
FUNCTION AND ANATOMY:

Explained previously

The major function of the lung is to replenish oxygen and remove carbon dioxide from blood.







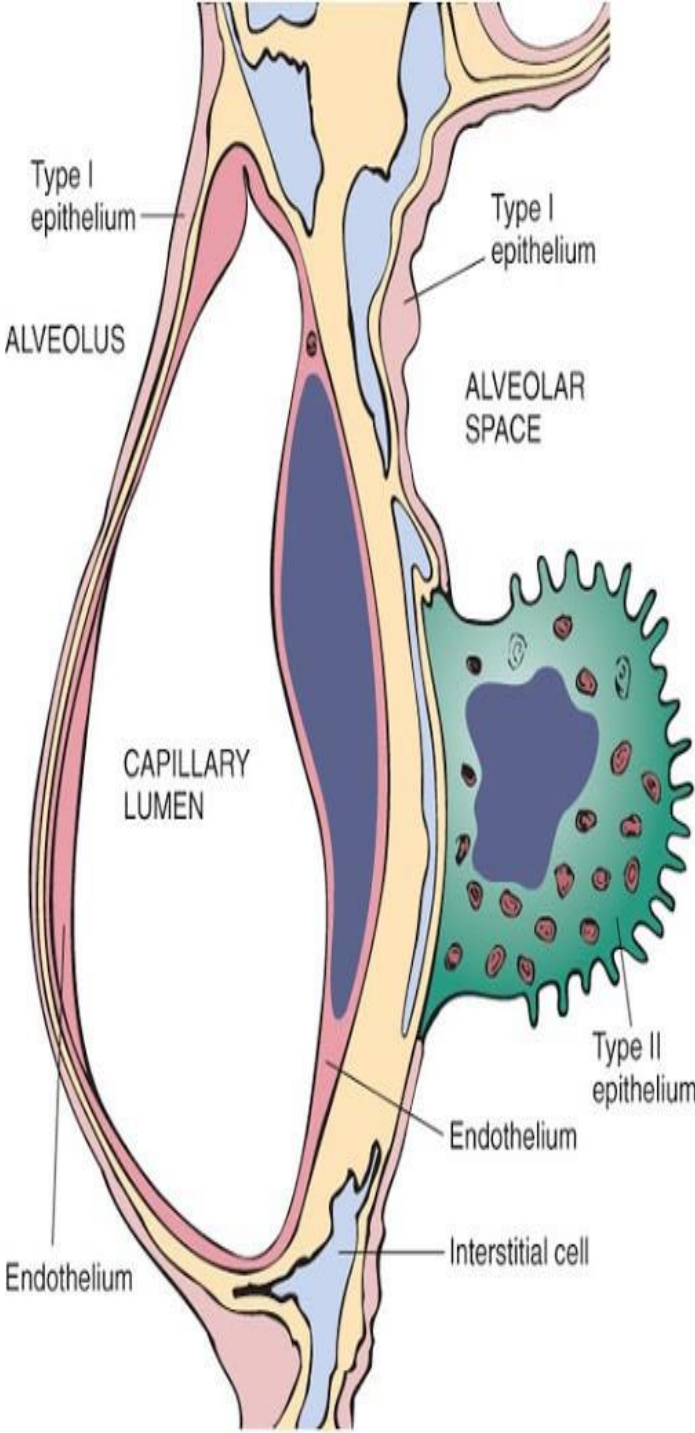
By TeachMeSeries Ltd (2019)https://teachmeanatomy.info/thorax/organs/tracheobronchial-tree/

The figure represents the alveolar wall and a capillary lined with endothelial cells embedded in it, which adapt the function of gases exchange.

We start the exchange process from the vascular side, so gasses should pass:

1) endothelial cells of the capillaries
2) basement membrane of the capillaries
3) The interstitium [contains fibroblast like cells, collagen fibers, elastic fibers, smooth muscles, and rare mononuclear cells], the Beig area
4) basement membrane of the alveoli
5) Alveolar lining epithelium(type 1 &2)
6) intra alveolar space, which has some pulmonary macrophages

This path is for both ways –entering and exiting the alveolus-



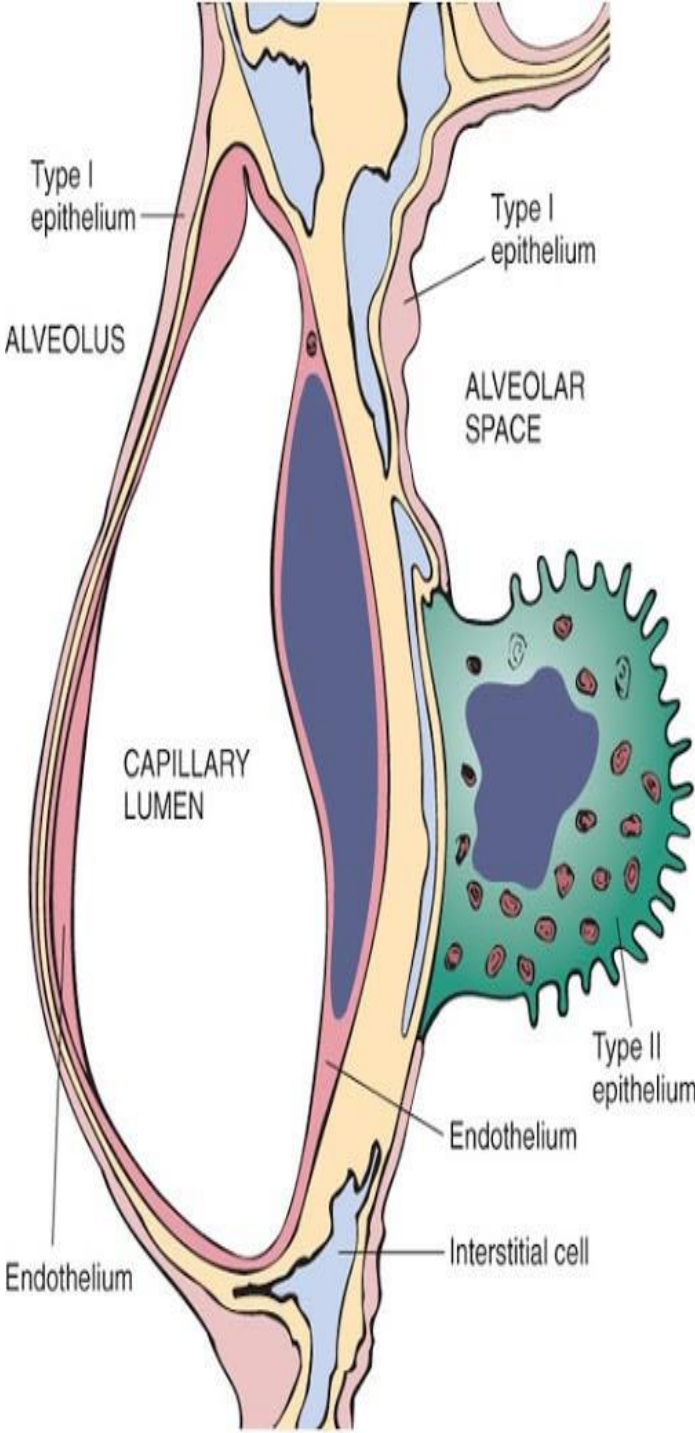
http://www.medicinehack.com/2011/05/microscopic-structure-of-alveolar-wall.html

So, what is the lining of alveoli?

Lined by 2 types of cells:

1) flattened, platelike cells, squamous epithelial cells called type 1 pneumocytes.
Responsible for the gases exchange process

2) rounded, hope nails shape, accounting for only 5% of the cells called type 2 pneumocytes.
Responsible for:
- producing surfactants which decrease surface tension between the air - fluid interface, to maintain alveoli patent especially during expiration
- regenerate and repair type 1 & 2 pneumocytes if there is any injury affecting the alveolar lining
- kill the pathogens

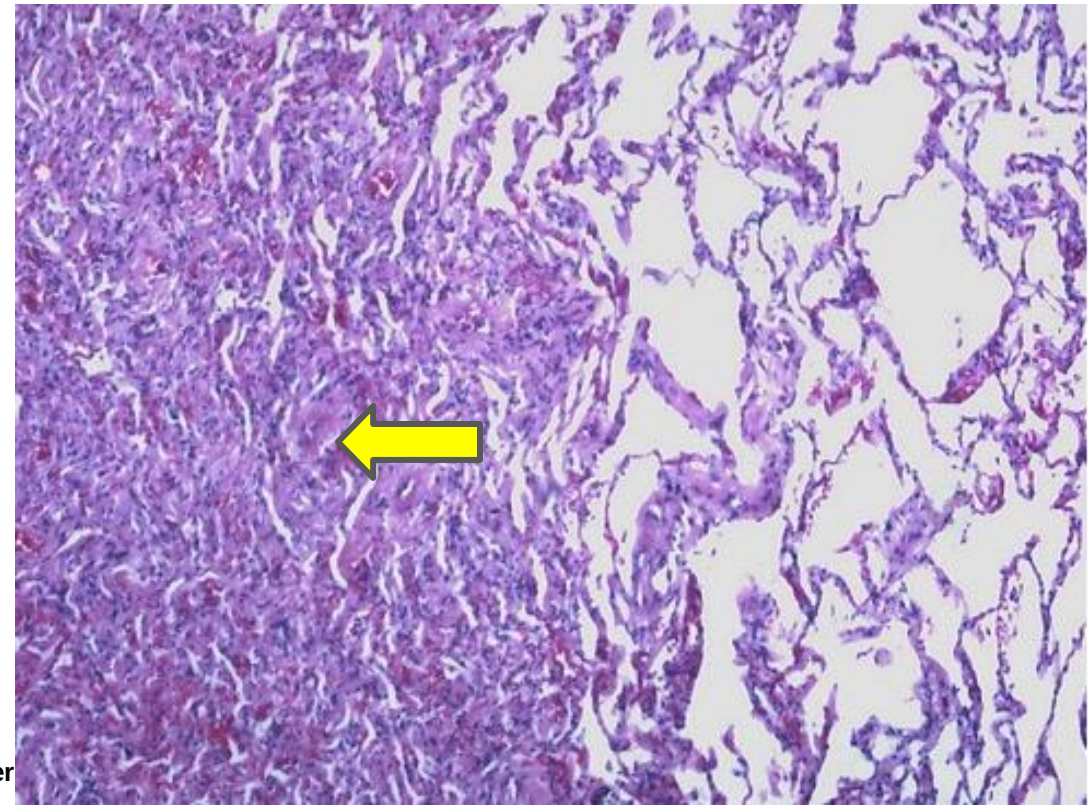


Topic 2
Atelectasis

This figure shows 2 different areas of the lung

On the right side we have many spaces filled with air, represents the normal lung where the alveoli are inflated by air
Also the thin lines represent the alveolar wall that we have discussed.

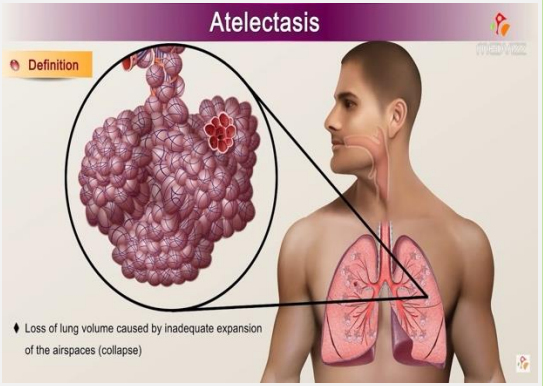
On the left side we have busy areas with low air or none, and loss of lung volume and this condition is called "Atelectasis" or "airless lung parenchyma"



https://teachmesurgery.com/per

Atelectasis: loss of lung volume caused by inadequate expansion of the air spaces (collapse) or airless lung parenchyma.

The ventilation-perfusion depends on how much volume of the lung is lost or affected , whether the entire lobe is affected, or the whole right lung, or only a focal area, If we have a significant volume collapse (airless), it results in shunting of inadequately oxygenated blood from pulmonary arteries into pulmonary veins and then into the systemic circulation reaching the tissues with low oxygen level leading to hypoxia.



The collapsed airway are at risk of infection

Atelectasis can be classified into:
1) neonatal Atelectasis due to low surfactants in premature babies
2) Acquired Atelectasis

Acquired Atelectasis can also be subclassified according to the mechanism into:
1) resorption or obstruction Atelectasis
2) compression Atelectasis
3) contraction Atelectasis (Cicatrization Atelectasis)

ATELECTASIS (COLLAPSE)

Explained previously

- is loss of lung volume caused by inadequate expansion of air spaces.

- It results in shunting of inadequately oxygenated blood from pulmonary arteries into pulmonary veins→ resulting in ventilation perfusion imbalance and hypoxia.

- The collapsed airway are at risk of infection

THREE TYPES OF ACQUIRED ATELECTASIS:

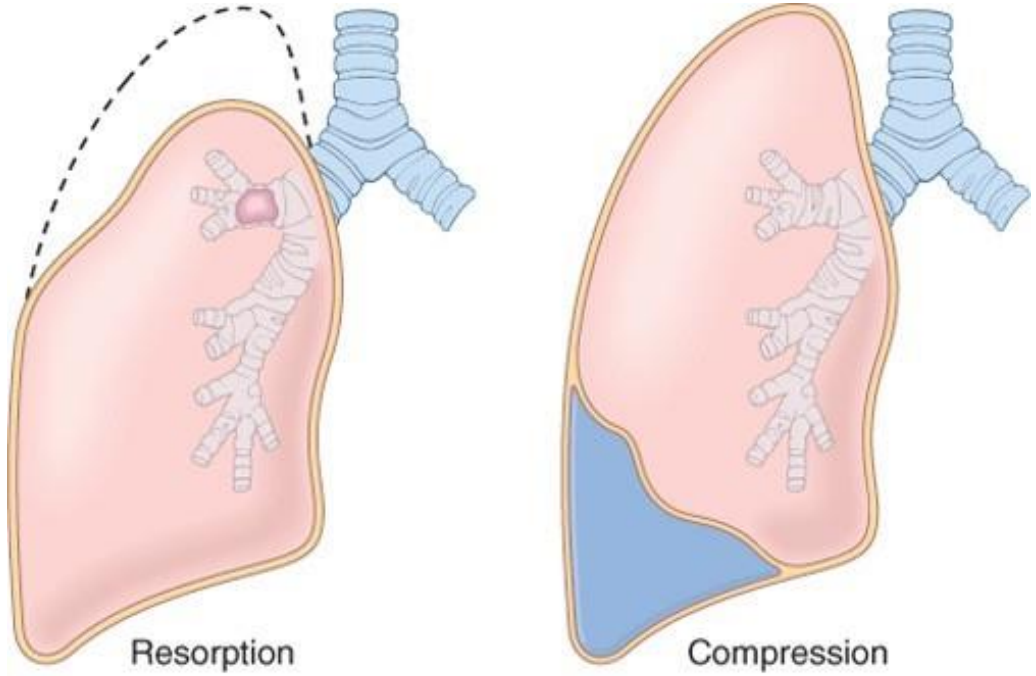
Explained previously

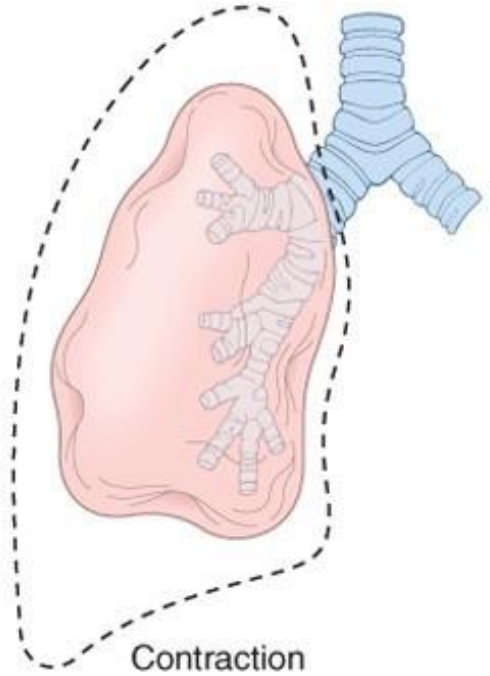
- Resorption atelectasis
- Compression atelectasis
- Contraction atelectasis (cicatrization atelectasis)

The dashed line represents the normal lung volume

The yellow line represents the real lung volume

In the 3 figures we have loss of lung volume

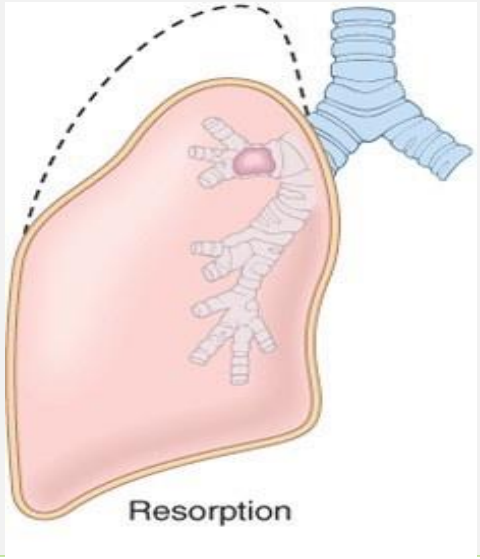




1. Resorption Atelectasis

Due to total obstruction of an airway (bronchi, segmental bronchi or terminal bronchi) preventing air from reaching the distal airways.

There is already some air in the distal airways but it is gradually resorbed by the continuous blood flow resulting in alveolar collapse.



Obstruction Causes:

1)intrabronchial mucous or mucopurulent plugs (common in post operative patients) are the most common causes.
with major surgeries like open heart surgery, it results in long hospital stay, decrease mobilization and long period under general anesthesia which causes respiratory drive suppression, also the patient will take shallow breath not deep one to avoid the pain caused by respiration. All these result in mucous accumulation, and usually this happens within 72 hrs after the major surgery.
So, there are some instructions we must do after surgery:
- Give the patient pain killers to encourage him to take deep breath.
- Make early mobilization and make the patient walk.
- Use spirometer, an instrument usually used to measure the inhalation and exhalation, but also used to exercise the lung by inhale and exhale high amount of air to get rid of mucus.

2)Foreign body aspiration especially in children when they play with legos or coins and a piece is inserted into one of the respiratory passages and depending on its size it will get stuck in a passage with a diameter smaller than its own. This blocks the airway and oxygen cannot reach the area beyond it causing sudden Suffocation and Atelectasis.
3)Obstructive lung disease: bronchial asthma, bronchiectasis, chronic bronchitis due to mucus production.
4)Intrabronchial tumors may cause complete obstruction.

Atelectasis Due to resorption is reversible once the obstruction is removed.

1.RESORPTION ATELECTASIS

Explained previously

- Due to total obstruction of an airway (bronchi, segmental bronchi or terminal bronchi) preventing air from reaching distal airways.

- The air already present in the distal airways gradually resorbed resulting in alveolar collapse.

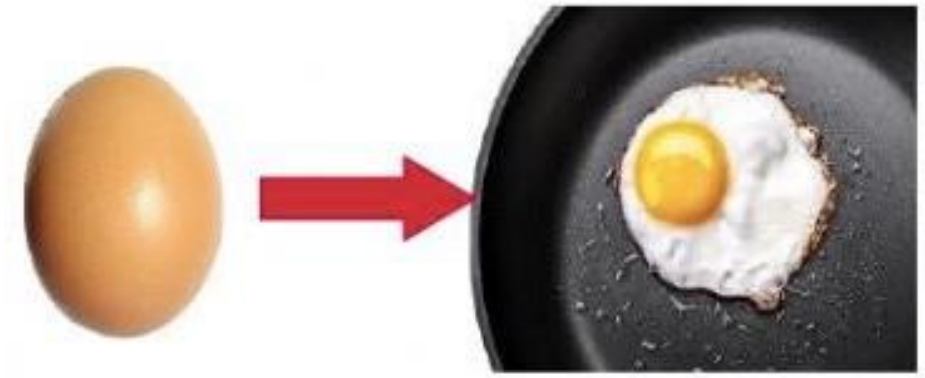
RESORPTION ATELECTASIS, CAUSED BY:

Explained previously

- **The most common cause is <u>Obstruction of a bronchus</u> by:**
  - ✓ Intrabronchial mucous or mucopurelant plugs in post operative patients.
  - ✓ Foreign body aspiration, especially in children
  - ✓ Obstructive lung disease: bronchialasthma, bronchiectasis, chronic bronchitis
  - ✓ Intrabronchial tumors.

Reversibility?

or



2. Compression Atelectasis

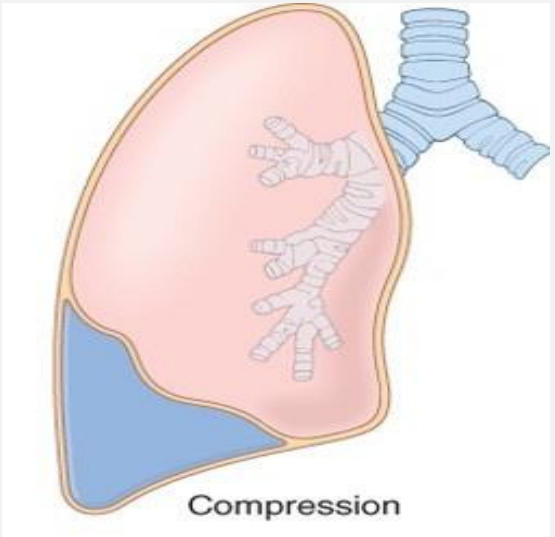
caused by the accumulation of significant amount of:

- fluids: like plural effusion in heart failure or blood from stabbing wounds or exudate or transudate.

- Air in pneumothorax: an abnormal collection of air in the pleural space between the lung and the chest wall.

- Solids: like tumor within plural cavity which mechanically collapses the adjacent lung.

Atelectasis caused by Compression is reversible, Once the fluid or air is a drained by inserting chest tube and by decreasing the pressure and mechanical force on the adjacent airways leading to inflation of the distal airways. Also by tumor removal surgery.



2. COMPRESSION ATELECTASIS

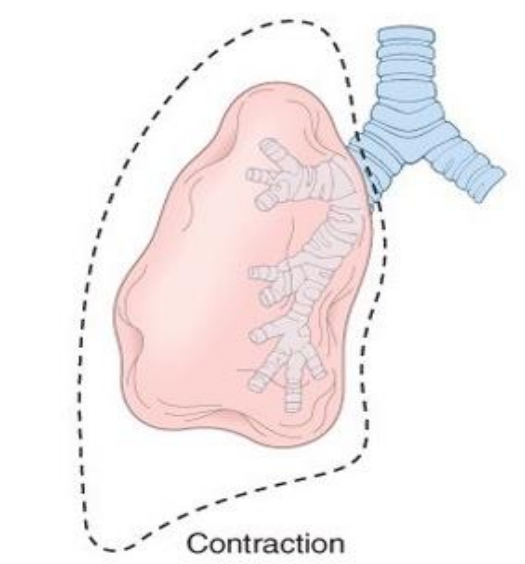
Explained previously

- caused by the accumulation of significant amount of fluid (blood, exudate or transudate), air (pneumothorax) or tumor within pleural cavity, which mechanically collapse adjacent lung (small airways and alveoli)
- E.x:
  a. Pleural effusion: in Congestive Heart Failure
  b. Pneumothorax: air in the pleural cavity due to RTA

3. Contraction Atelectasis (Cicatrization Atelectasis)

It can be focal or diffused by fibrosis or scarring of the lung or pleura causing changes in the architecture and prevents full expansion of the lung leading it to collapse.

Atelectasis caused by contraction is not reversible due to fibrosis.



Explained previously

3. CONTRACTION ATELECTASIS (CICATRIZATION ATELECTASIS)

- Occurs due to local or generalized fibrosis/scarring of the lung or pleura that prevents full expansion of the lung

Topic 3
Acute Respiratory Distress Syndrome

An example of ARDS happens in corona, some patients were in good health, but suddenly they experience a deterioration that requires hospitalization, oxygen therapy, and sometimes intensive care units (ICU). Some patients died due to this deterioration, while others survived but with permanent complications in the pulmonary functions.

The definition of ARDS is evolving, but the simplest definition is sudden onset of respiratory failure leading to low O2 or high CO2 or both, occurring within 1 week of a known clinical insult [the list is very long such as: COVID-19, sepsis, gastric bypass surgery,…. and so on]

So, if your patient have known disease and hospitalized due to it, and suddenly they call you and tell you that your patient is deteriorating -within one week- and developed shortness of breath (dyspnea).

Then you should do ABG test (arterial blood gases) to evaluate O2 & CO2 & pH from arterial blood sample. Then you find that he has respiratory failure [decrease O2 with or without increase CO2 according to the respiratory failure type] and radio densities or bilateral opacities meaning white lungs in the x-rays.

ARDS Is not fully explained by effusions, Atelectasis, cardiac failure or fluid overload, you should also exclude cardiac causes before diagnosing him with ARDS, If all these are excluded then you diagnose him with ARDS.

ARDS is the severe end of the spectrum of acute lung injury .

Acute lung injury: is sudden onset of hypoxia and bilateral pulmonary edema in the absence of cardiac causes (non cardiogenic)

The histological manifestation of this disease is called diffuse alveolar damage (DAD), the lining epithelium of the alveoli is damaged, which is responsible of the symptoms like hypoxia, dyspnea and respiratory failure.

ARDS Graded based on the severity of the changes in arterial blood oxygenation into mild moderate and severe. remember the ABG test, increase O2 deficiency —> more severe ARDS

Severe ARDS characterized by rapid onset of life-threatening respiratory insufficiency, cyanosis, multisystem organ failure, severe arterial hypoxemia that becomes refractory to oxygen therapy due to DAD, type 1 pneumocytes which responsible for gases exchange are damaged, so you give O2, but there are no enough cells to do gases exchange.

Explained previously

ACUTE RESPIRATORY DISTRESS SYNDROME (ARDS)

- **ARDS defined as** respiratory failure occurring within 1 week of a known clinical insult with bilateral opacities on chest imaging, NOT fully explained by effusions, atelectasis, cardiac failure, or fluid overload.
- considered to be the severe end of a spectrum of acute lung injury
- The histologic manifestation of this disease is called **diffuse alveolar damage (DAD)**

ARDS

Explained previously

- graded based on the severity of the changes in arterial blood oxygenation into mild, moderate and sever
- Sever ARDS characterized by rapid onset of life-threatening **respiratory insufficiency, Cyanosis , Severe arterial hypoxemia that becomes refractory to oxygen therapy and may progress to multisystem organ failure**

This table summarizes the most common conditions that associated with the development of ARDS, but the list is longer.

You should memorise:

- Sepsis
- Diffuse pulmonary infections,
including bacterial, viral like COVID-19, fungal
- Gastric Aspiration
- Mechanical trauma including head injuries

Table 15.2 Conditions Associated With Development of Acute Respiratory Distress Syndrome

Infection
Sepsis[a]
Diffuse pulmonary infections[a]
Viral, *Mycoplasma*, and *Pneumocystis* pneumonia; miliary tuberculosis
Gastric aspiration[a]
Physical/Injury
Mechanical trauma including head injuries[a]
Pulmonary contusions
Near-drowning
Fractures with fat embolism
Burns
Ionizing radiation
Inhaled Irritants
Oxygen toxicity
Smoke
Irritant gases and chemicals
Chemical Injury
Heroin or methadone overdose
Acetylsalicylic acid
Barbiturate overdose
Paraquat
Hematologic Conditions
Transfusion-associated lung injury (TRALI)
Disseminated intravascular coagulation
Pancreatitis
Uremia
Cardiopulmonary Bypass
Hypersensitivity Reactions
Organic solvents
Drugs

[a]More than 50% of cases of acute respiratory distress syndrome are associated with these four conditions.

ARDS should not be confused with respiratory distress syndrome of the newborn; the latter is caused by a deficiency of surfactant caused by prematurity.

PATHOGENESIS

Simply is inflammation, and The heroine of the story is the neutrophils.

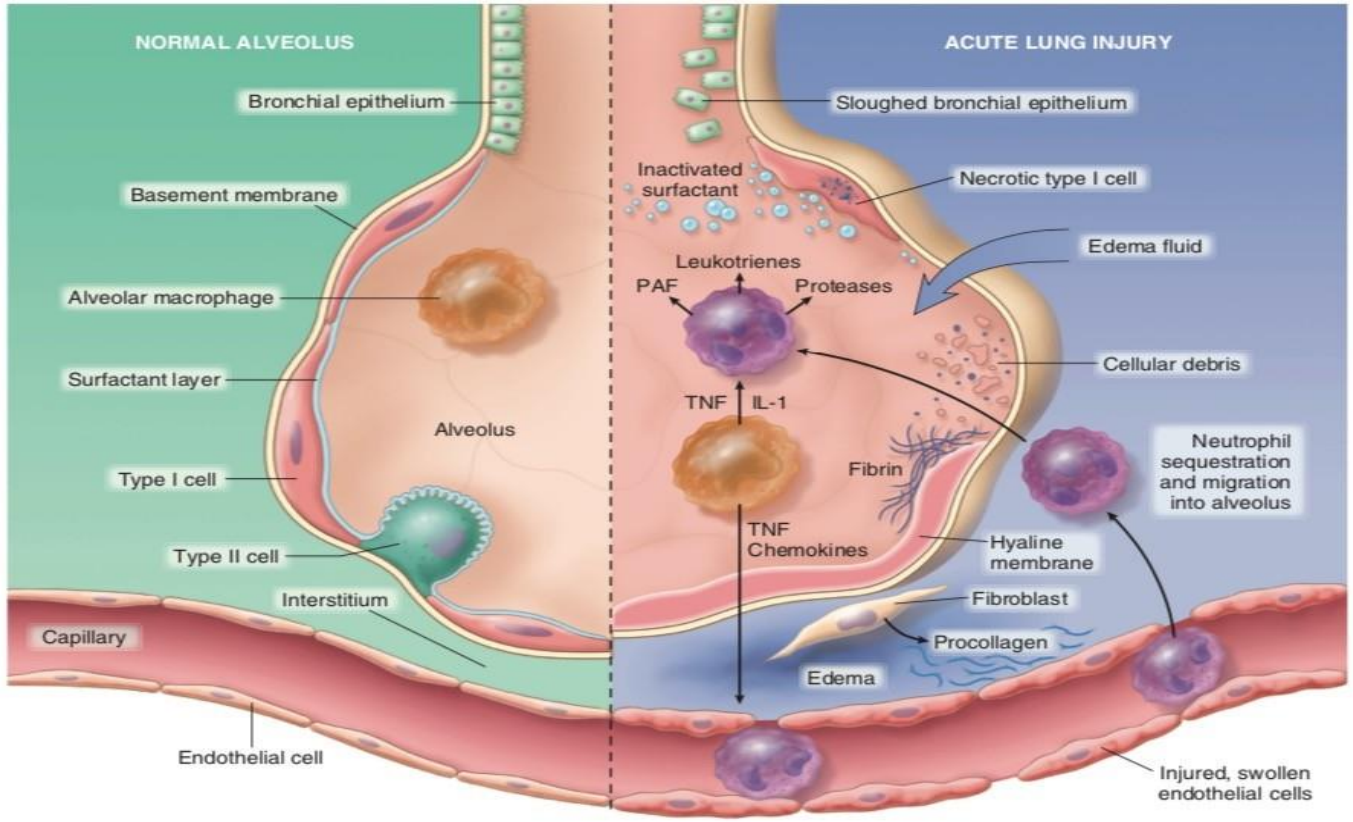
NORMAL ALVEOLI

The wall is lined by type 1 and few of type 2 pneumocytes

Clean intra alveolar space contains only one macrophage

Capillary embedded within the wall lined by endothelial cells with tight junctions and contains blood

The green area represents the interstitium



Represents inflammation in ARDS

As early as 30 minutes after an acute trigger insult, there is an activation of intra alveolar pulmonary macrophages either directly or indirectly.
An example of direct activation is pneumonia which causes damage to type 1 & 2 cells and they will release mediators.
An example of indirect activation is pancreatitis, resulting in pancreatic enzymes release into the systemic circulation which will initiate inflammatory reaction reaching the lungs.

So, there is an increase in the synthesis and release of mediators like IL-8, IL-1, and TNF by pulmonary macrophages. These mediators lead to endothelial activation and sequestration, expression of adhesion molecules and they also increase the vascular permeability by increasing gaps between the endothelial cells which will facilitate the leakage of fluid into the interstitium. They also work as chemotactic factors(signals) which attract neutrophils leading to their activation ,neutrophils will then exit the circulation and enter the intra alveolar space.

Activated neutrophils degranulate and release the reactive oxygen species, proteases, leukotrienes and PAF that further damage the alveolar epithelium and endothelium causing vascular weakness and cause damage to type 1 cells --> decrease gases exchange, and type 2 cells damage -->reduce surfactants.

Furthermore, the damage will result in leakage of Edema fluid from intravascular compartments to the intra alveolar compartment and washing the surfactants that already have been there. So, this alveolus will collapse.

Another effect is the accumulation of homogeneous pink, fibrin rich edema fluid admixed with remnants of necrotic epithelial cells called hyaline membrane -collected at the alveolar wall-

Hyaline membrane is a characteristic feature of acute ARDS phase, not in organized phase.

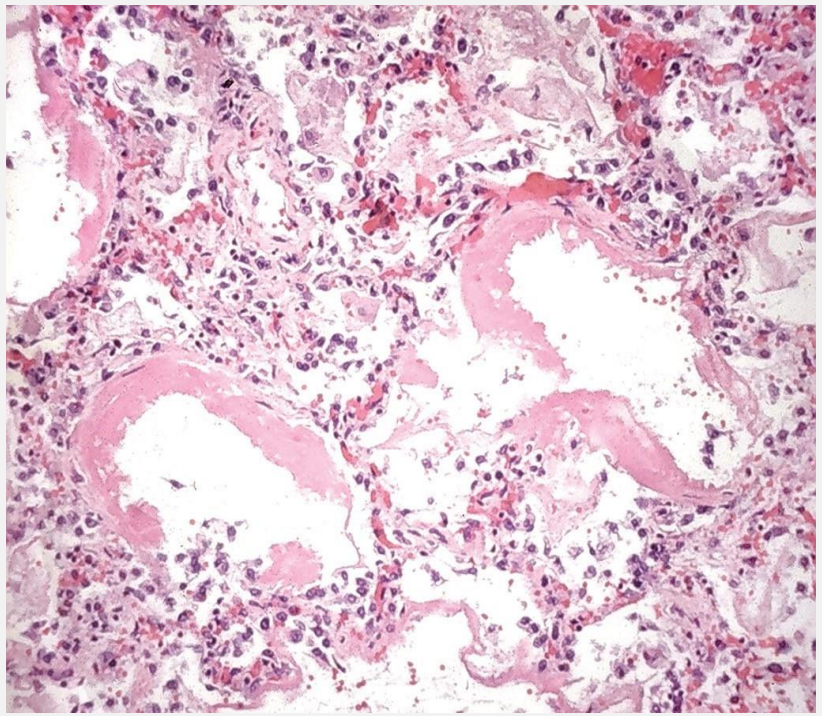
Our body fights this process and prevents its continuation by releasing protective factors, including anti proteases and antioxidants. So the outcomes differ between the patients depending on the balance between the destructive forces of the cytokines from the neutrophils and the protective forces of our body like anti proteases and antioxidants. Also, the severity of ARDS depends on this balance.

If protective factors succeeded the damage will stop then we start the organization or healing phase.

In the acute phase:

Many alveoli are collapsed due to type 2 cells damage and low surfactants

the few preserved cells lining with hyaline membrane



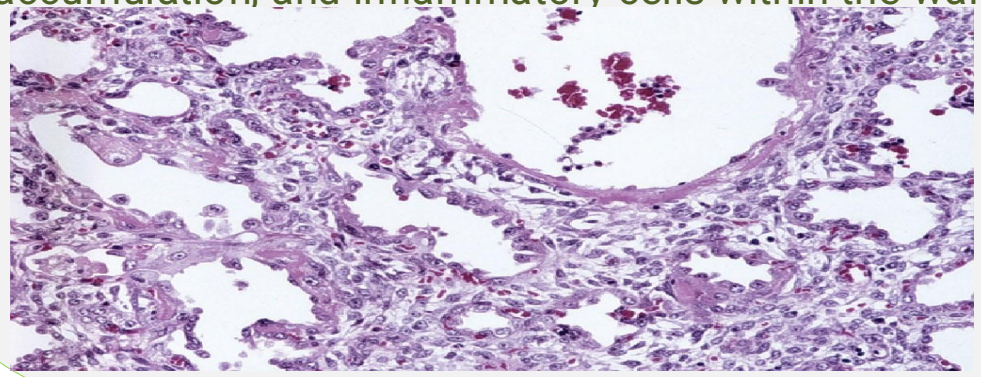
In the organization phase:

Hyperplasia of type 2 cells to replace type 1 & 2

Pulmonary macrophages engulf all debris and fluid accumulation including the hyaline membrane.(No hyaline membrane)

Pulmonary macrophages release fibrogenic factors like TGF-B and PDGF to stimulate collagen deposition leading to healing by fibrosis within the alveolar wall leading to wall thickness

The residual endothelial cells will proliferate and replace the damaged cells, note the expanded alveolar wall due to fibroblast proliferation, collagen accumulation, and inflammatory cells within the wall



PATHOGENESIS:

Explained previously

- the integrity of the alveolar-capillary membrane is compromised by endothelial and epithelial injury.

- As early as 30 minutes after an acute insult, there is increased synthesis and release of IL-8, IL-1 and TNF by pulmonary macrophages.

- leading to endothelial activation and sequestration
- activation & chemotaxis of neutrophils in pulmonary capillaries.

PATHOGENESIS/CONT.

Explained previously

- Activated neutrophils release reactive oxygen species & proteases that damage the alveolar epithelium and endothelium causing vascular leakiness and loss of surfactant that render the alveolar unit unable to expand.

- the destructive forces are counteracted by endogenous anti-proteases and anti-oxidants

Explained previously

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

HISTOLOGY:

Explained previously

- In the acute phase of ARDS :

  - The most characteristic finding is the presence of **hyaline membranes**

  - consists of fibrin-rich edema fluid admixed with remnants of necrotic epithelial cells

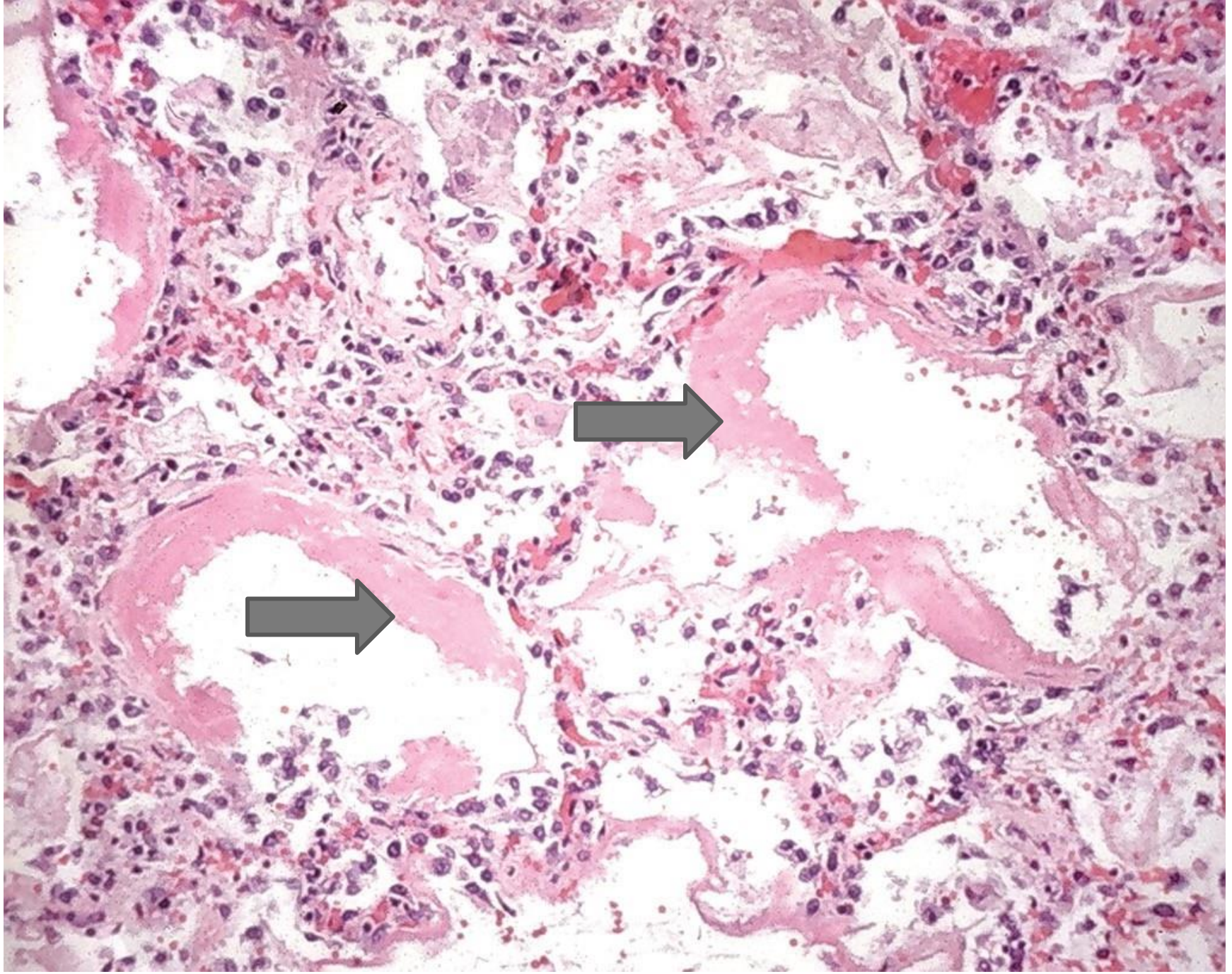


FIGURE 13.3A,ROBBINS BASIC PATHOLOGY, 10TH EDITION

HISTOLOGY:

Explained previously

In the organizing stage:

- **proliferation of type II pneumocytes**
- **intraalveolar fibrosis** due to organization of the fibrin-rich exudates.
- **Marked thickening of the alveolar septa due to proliferation of interstitial cells and collagen deposition.**

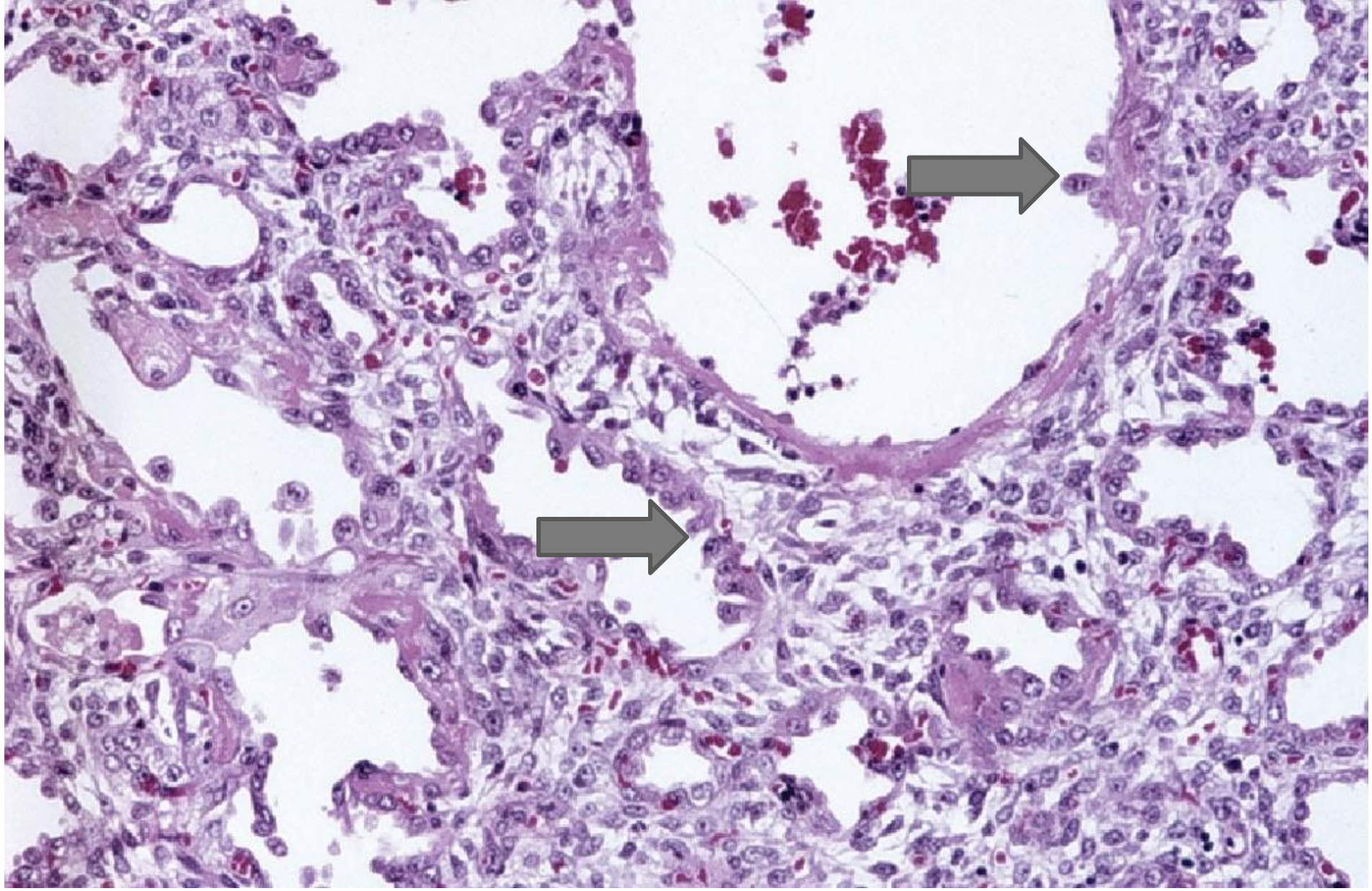


FIGURE 13.3B,ROBBINS BASIC PATHOLOGY, 10TH EDITION

CLINICAL FEATURES

Explained previously

- Patients are hospitalized for one of the predisposing conditions

- Profound *dyspnea and tachypnea* followed by increasing *cyanosis and hypoxemia*, *respiratory failure*, and the appearance of *diffuse bilateral infiltrates* on radiographic examination.

- Hypoxemia may be refractory to oxygen therapy due to ventilation-perfusion mismatch, and respiratory acidosis can develop.

OUTCOME:

- The overall hospital mortality rate is 38.5%. more than 1/3 will not survive
- The majority of deaths are attributable to sepsis, multiorgan failure, or severe lung injury.
- Most patients who survive the acute insult recover normal respiratory function within 6 to 12 months, but the rest have lung damage resulting in interstitial fibrosis and chronic pulmonary disease.

PREDICTORS OF POOR PROGNOSIS

1. Advanced age >80 years
2. bacteremia (sepsis) ,cytokines storm
3. development of multiorgan failure if the pts have it or it happened during the illness like heart & renal failure

Topic 4
Diffuse Pulmonary Diseases

- **OBSTRUCTIVE AIRWAY DISEASES:** characterized by an increase in resistance to airflow caused by partial or complete obstruction at any level

- **RESTRICTIVE DISEASES:** characterized by reduced expansion of lung parenchyma and decreased total lung capacity.

Restrictive defects occur in:

- **chest wall disorders in the presence of normal lungs:**

severe obesity, diseases of the pleura limiting lung expansion, and neuromuscular disorders that affect the respiratory muscles like Guillain barre syndrome.

- **acute or chronic interstitial lung diseases**:
  - The classic typical **acute** restrictive disease is **ARDS**.
  - Chronic restrictive diseases include the pneumoconiosis, interstitial fibrosis of unknown etiology, and sarcoidosis.

Topic 4

Explained previously

DIFFUSE PULMONARY DISEASES can be classified into two Categories:

1 **OBSTRUCTIVE AIRWAY DISEASES:** characterized by an increase in resistance to airflow caused by partial or complete obstruction at any level

2 **RESTRICTIVE DISEASES:** characterized by reduced expansion of lung parenchyma and decreased total lung capacity.

Restrictive defects occur in two general conditions:

Explained previously

1. **chest wall disorders in the presence of normal lungs:**
   - severe obesity, diseases of the pleura , and neuromuscular disorders that affect the respiratory muscles

2. **acute or chronic interstitial lung diseases**:
   - The classic **acute** restrictive disease is **ARDS**.
   - **Chronic restrictive diseases** include the **pneumoconioses, interstitial fibrosis of unknown etiology, and sarcoidosis**.

A 58-year-old man with ischemic heart disease undergoes coronary artery bypass graft surgery under general anesthesia. Two days postoperatively, he experiences increasing respiratory difficulty with decreasing arterial oxygen saturation. On physical examination, his heart rate is regular at 78/min, respirations are 25/min, and blood pressure is 135/85 mmHg. The hemoglobin concentration has remained unchanged, at 13.7 g/dL, since surgery. After he coughs up a large amount of mucoid sputum, his condition improves. Which of the following types of atelectasis does he most likely have?

A) Compression

B) Contraction

C) Resorption

A 58-year-old man with ischemic heart disease undergoes coronary artery bypass graft surgery under general anesthesia. Two days postoperatively, he experiences increasing respiratory difficulty with decreasing arterial oxygen saturation. On physical examination, his heart rate is regular at 78/min, respirations are 25/min, and blood pressure is 135/85 mmHg. The hemoglobin concentration has remained unchanged, at 13.7 g/dL, since surgery. After he coughs up a large amount of mucoid sputum, his condition improves. Which of the following types of atelectasis does he most likely have?

reverasble

A) Compression

B) Contraction

C) Resorption

Let’s summarize the lecture in two slides🔻

Atelectasis: loss of lung volume

Resorption	**Compression**	**Contraction (Cicatrization)**
Obstruction: - Post operative - Foreign body - Obustructive lung diseases - tumor	Accumulation of fluids, air (pneumothorax), solid	Fibrosis
Mediastinum shifts toward the atelectatic lung	Mediastinum shifts away from the atelectatic lung	
Reversible	Reversible	Not reversible

ARDS: respiratory failure

Causes	Key words	Symptoms	Predictors of poor prognosis
Sepsis Diffuse pulmonary infection Gastric aspiration Mechanical trauma including head injury " Pts already hospitalized"	Inflammation Neutrophils DAD diffuse alveolar damage Extensive bilateral injury Radio densities	Respiratory insufficiency Cyanosis Dyspnea Tachypnea Arterial hypoxemia refractory to O2 therapy	Age Sepsis Multiorgan failure

Acute phase	Organized phase
Hyaline membrane: fibrin rich edema fluid with necrotic epithelial cells remnant	Type 2 hyperplasia Thickening of alveolar wall due to fibrosis No hyaline membrane

Additional sources

1. Book pages
2. Youtube videos
3. Webpages…etc

آية أو حديث شريف دعاء أو نصيحة .....
اترك أثر جميل للقارئ

VERSIONS	SLIDE #	BEFORE CORRECTION	AFTER CORRECTION
V1→ V2	30	Type 2 and few type 1	Type 1 and few type 2
V2→V3	31	13	30

امسح الرمز و شاركنا بأفكارك لتحسين أدائنا !!