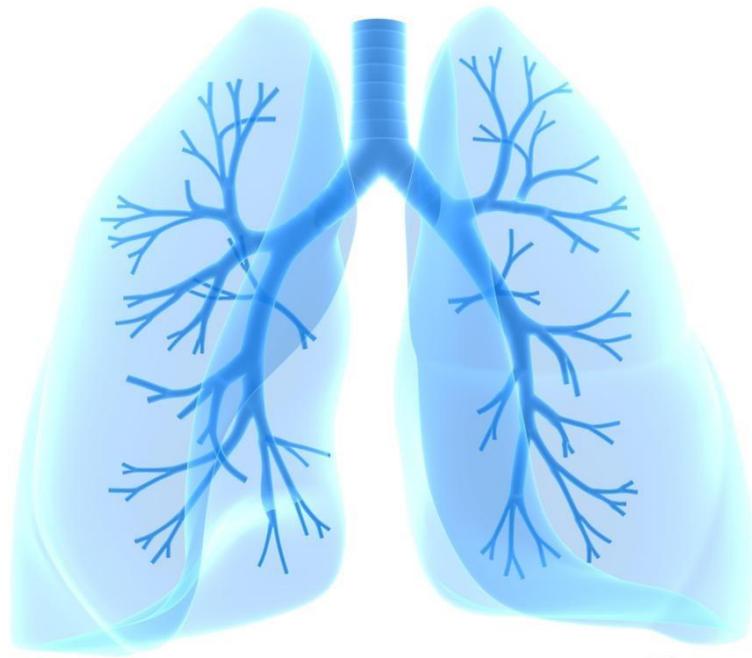


# Respiratory Pathology

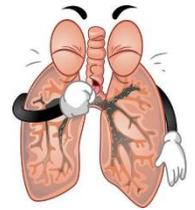


Lecture 1

Done by : Omar Rashdan

Doctor : Maram

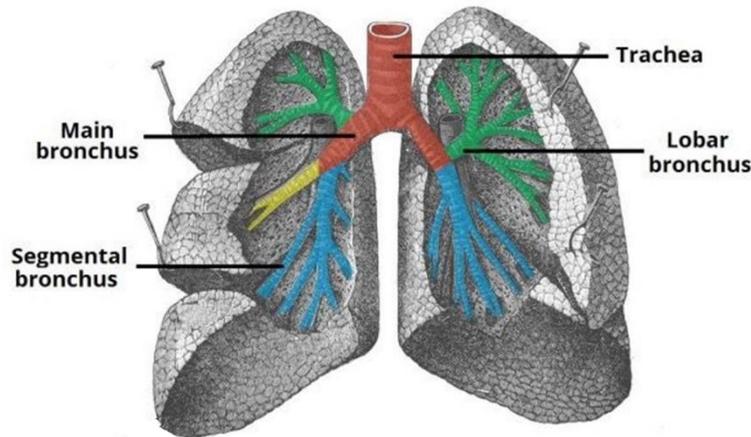
# Respiratory System



## ❁ Function of the respiratory system

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

## ❁ Anatomy of the respiratory system



- This figure shows the tracheobronchial tree and the lung's anatomy . The midline trachea marks the beginning of the tracheobronchial tree , then , at the level of the sternal angle , the trachea bifurcates into the left and right main (primary bronchi).

- The **right main bronchus subdivides into three lobar bronchi** (the right lungs contains three lobes) and the **left main bronchus subdivides into two lobar bronchi** (the left lung contains two lobes).

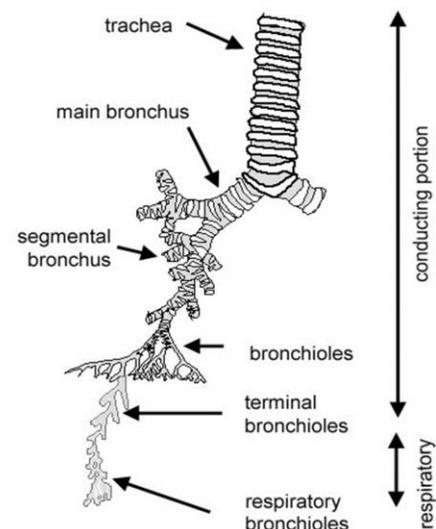
- The lobar bronchi further subdivide into smaller branches (airways) called bronchioles.

**Important Note** : Bronchioles are distinguished from bronchi by the lack of cartilage and submucosal glands within their walls.

- Additional branching of the bronchioles leads to the terminal bronchioles.

- The part of the lung distal to the terminal bronchiole is called the **Pulmonary Acinus**.

- **Pulmonary Acini** are composed of respiratory bronchioles branching from the terminal bronchiole that proceed into alveolar ducts which immediately branch into the alveolar sacs.

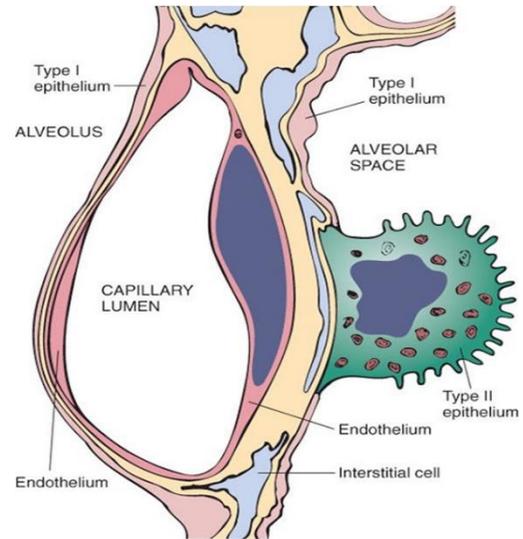


- **The alveolar sacs** are the blind end of the respiratory passages , and their walls are formed entirely by alveoli which is the ultimate site of gas exchange. (**Clusters of alveoli**)

- The figure on the right represents the alveolar wall (alveolar septa) and its components , the blood side (capillary) on the left and air side (alveolus) on the right.

- The wall (6 layers) starts with the

- (1) the capillary endothelium ,
- (2) resting on a basement membrane ,
- (3) separated from the alveolus by the interstitium ,
- (4) followed by alveolar basement membrane ,
- (5) on which the alveolar epithelial cells rest ,
- (6) the surfactant layer



- The alveolar epithelium is made of a continuous layer of two cell types :

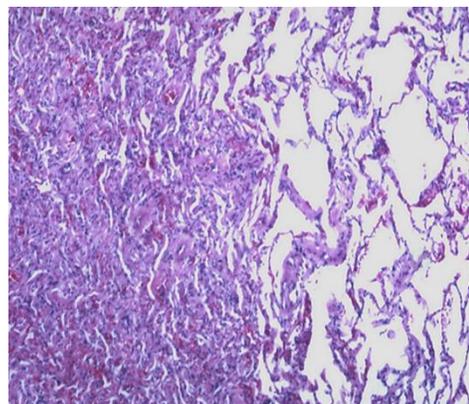
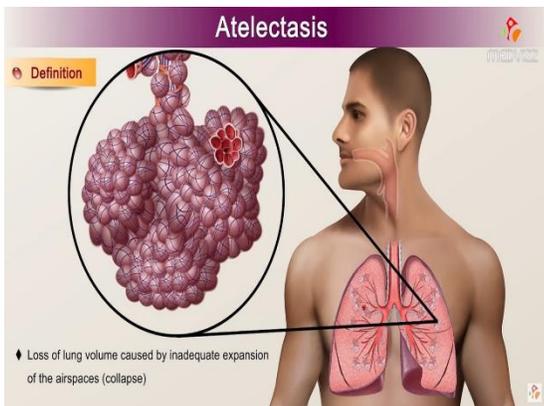
- I. Type I pneumocytes (type 1 epithelium) : flattened epithelial cells covering about 95% of the alveolar surface.
- II. Type II pneumocytes (type 2 epithelium) : rounded epithelial cells which function to produce the pulmonary surfactant . They are the main cells involved in the repair of alveolar epithelium following type I pneumocytes damage.

- Few alveolar macrophages are usually seen within the alveolar spaces ; these alveolar macrophages and mononuclear cells are present free in the alveolar space.

## Atelectasis (collapse)

**Definition** : loss of lung volume caused by **inadequate expansion of air spaces**.

**It results in** shunting of inadequately oxygenated blood from pulmonary arteries into veins, thus giving rise to a ventilation-perfusion imbalance and hypoxia.

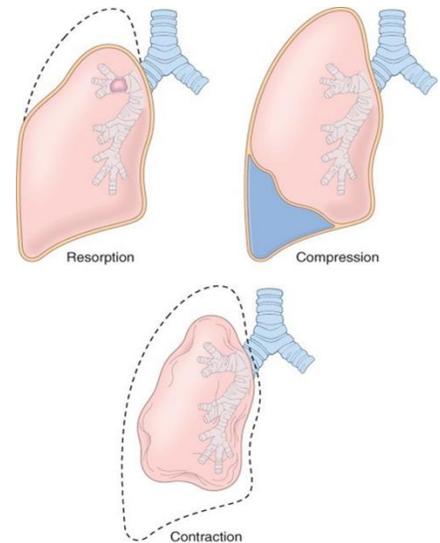


In this figure , the left side of the picture shows airway collapse due to atelectasis.

Based on the underlying mechanism and the distribution of alveolar collapse, atelectasis can be classified into **three types** :

- 1) Resorption atelectasis
- 2) Compression atelectasis
- 3) Contraction atelectasis (cicatrization atelectasis)

The figure on the right represents the three types of atelectasis, the dashed lines highlight the normal lung volume.



### 1) Resorption atelectasis :

#### ➤ Mechanism :

- Happens due to total obstruction of a bronchus preventing outside air from reaching distal airways.
- The air already present gradually becomes absorbed, and alveolar collapse follows.
- Airway obstruction occurs in bronchi, segmental bronchi or terminal bronchi.

#### ➤ Cause of resorption atelectasis :

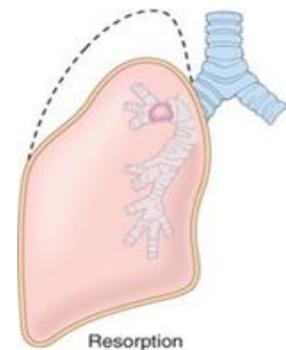
The most common cause is obstruction of a bronchus by:

- Intrabronchial mucous or mucopurulent plugs in post operative patients (especially in the first 72 hours).

**Note** : that's why we encourage our patients to take deep breaths and use the spirometer.

- Foreign body aspiration, especially in children because children have poorly developed collaterals for ventilation.
- Obstructive lung disease: bronchial asthma, bronchiectasis, chronic bronchitis
- Intrabronchial tumors.

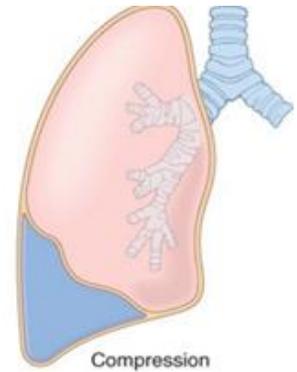
**Note** : atelectasis due to resorption is **reversible** once the obstruction is removed.



## 2) Compression atelectasis :

### ➤ Mechanism :

- Caused by accumulation of fluid, blood, or air within the pleural cavity.
- The increased pressure will result in mechanical collapse of the adjacent lung (small airways and alveoli)



### ➤ Examples/causes :

- Pleural effusion : like in patients with **Congestive Heart Failure**.
- Pneumothorax : air in the pleural cavity after a **Chest penetrating injury**. Both can increase the pressure and compress the adjacent lung.

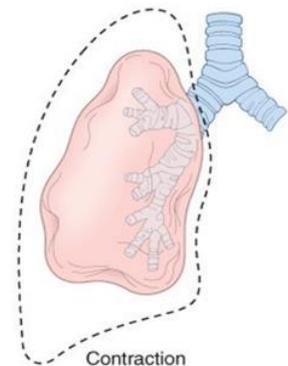
**Note** : atelectasis caused by compression is **reversible** once the fluid/air is drained.

## 3) Contraction atelectasis :

### ➤ Mechanism :

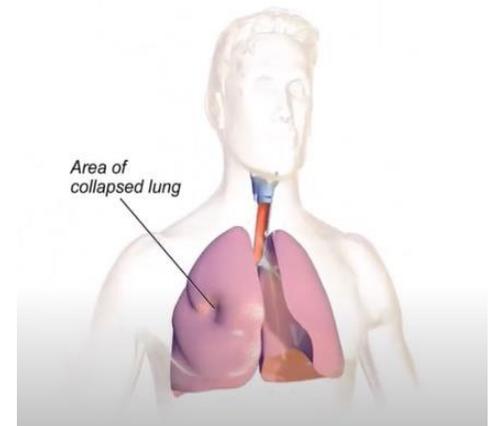
- Occurs due to local or generalized **fibrosis** of the lung or pleura that prevents full expansion of the lung.

**Note** : atelectasis caused by contraction is **not reversible** due to fibrosis.



## Summary

- ❖ Atelectasis (except when caused by contraction) is potentially reversible and should be treated promptly to prevent hypoxemia and superimposed infection of the collapsed lung.
- ❖ As shown in the figure on the right , the expansion of air spaces is inadequate in atelectasis.
- ❖ Since the expansion of the air spaces is limited , the lung volume available for gas exchange is decreased.
- ❖ Final result is , shunting of inadequately oxygenated blood from pulmonary arteries into veins, thus giving rise to a ventilation-perfusion imbalance and hypoxia.
- ❖ Again , atelectasis is potentially reversible except when caused contraction.



## ACUTE RESPIRATORY DISTRESS SYNDROME (ARDS)

### ➤ General information :

- ✧ The epidemiology and definition are evolving.
- ✧ Formerly considered to be the severe end of a spectrum of acute lung injury.
- ✧ Nowadays , it is defined as respiratory failure occurring within 1 week of a known clinical insult with bilateral opacities on chest imaging.

These findings are **not** fully explained by effusions, atelectasis, cardiac failure, or fluid overload.

- ✧ So , ARDS is a respiratory failure where the respiratory system fails in one or both of gas exchange functions , i.e. oxygenation and elimination of carbon dioxide (CO<sub>2</sub>).
- ✧ ARDS is graded based on the severity of the changes in arterial blood oxygenation.
- ✧ **Causes are diverse however they share a common feature which is extensive bilateral injury to alveoli known histologically as diffuse alveolar damage (DAD).**

### ➤ ARDS triggers :

- ✧ Pneumonia (35%–45%).  
**Note : the most frequent triggers for ARDS are infections (including covid-19).**
- ✧ Sepsis (30%–35).
- ✧ Aspiration.
- ✧ Trauma (including brain injury, abdominal surgery, and multiple fractures).
- ✧ Pancreatitis.
- ✧ Transfusion reactions.

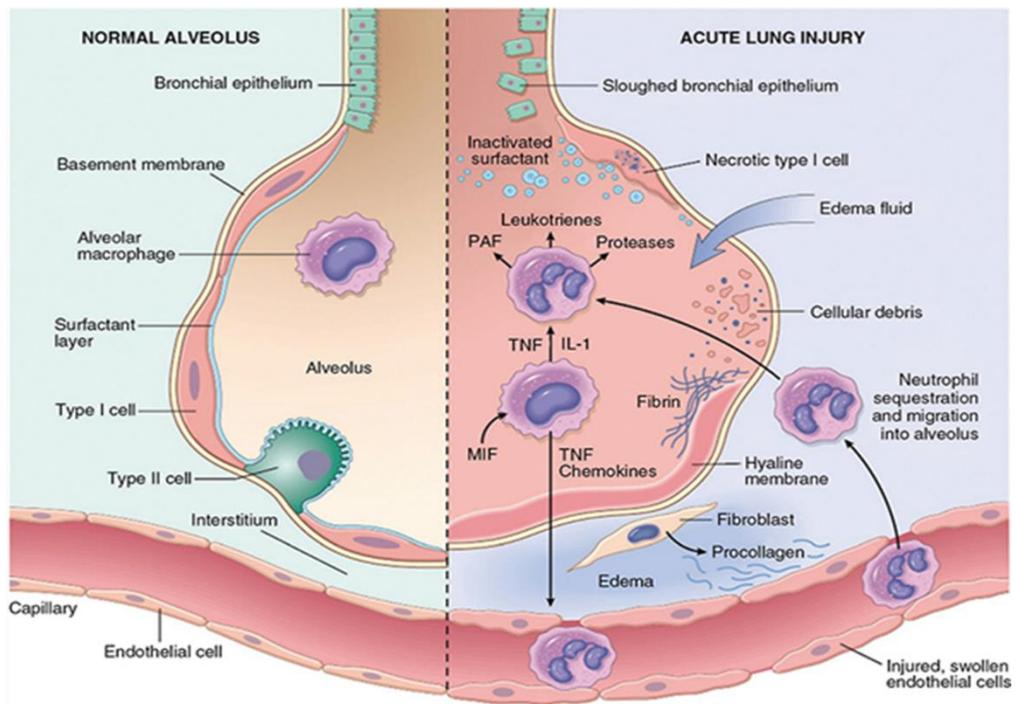
### ➤ Characterization :

**Severe ARDS is 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.

**Important note :** 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 of ARDS:



This figure compares between a normal alveolus on the left vs an injured alveolus on the right.

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

### Steps :

- 1) In the early phase of ARDS , about 30 minutes after the acute insult caused by any of the triggers mentioned before , pulmonary macrophages increase their synthesis and release of IL-1 , IL-8 , TNF and other factors.
- 2) These factors result in neutrophils chemotaxis , sequestration , activation , and then migration into the alveolus.
- 3) Also , endothelial cells in the pulmonary capillaries are activated.
- 4) The activated neutrophils release reactive oxygen species (ROS) , leukotrienes , proteases , and platelet activating factor (PAF) that damage both alveolar epithelium and capillary endothelium.
- 5) Damage to the alveolar epithelium and capillary endothelium cause vascular leakiness (accumulation of edema fluid) , loss of surfactant (surfactant inactivation) and hyaline membrane formation.
- 6) All the previous changes **render the affected alveolar unit unable to expand.**

### Important :

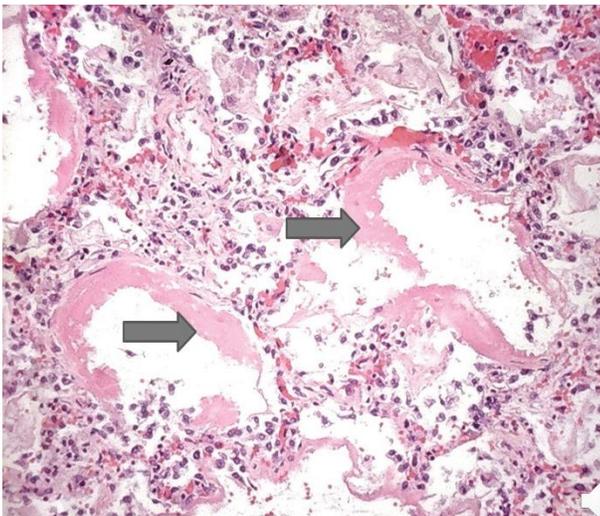
- ✓ During this process , destructive forces are counteracted by the release of endogenous anti-proteases and anti-oxidants
- ✓ In the end, it is the balance between the destructive and protective factors that determines the degree of tissue injury and clinical severity of the ARDS.
- ✓ Then , the macrophages start releasing fibrogenic cytokines including transforming growth factor  $\beta$  (TGF- $\beta$ ) and platelet derived growth factor (PDGF) stimulating fibroblasts growth and collagen deposition which is associated with the healing stage of the injury.
- ✓ Note : with everything said , one concludes that neutrophils play an important role in the pathogenesis of ARDS.
- ✓ Neutrophils activation by pulmonary macrophages is essential in the pathogenesis of ARDS.

Even early lung biopsies of affected patients shows an increased number of neutrophils within the vascular spaces , interstitium , and the alveoli.

### ➤ Histology:

#### In the acute phase of ARDS :

- The lungs are dark red , firm , airless and heavy.
- Upon microscopic examination , capillary congestion , necrosis of alveolar epithelial cells , interstitial and intra-alveolar edema and hemorrhage and collections of neutrophils in the capillaries are seen.
- However , the most characteristic finding is the presence of hyaline membranes.
- Hyaline membranes consist of fibrin-rich edema fluid admixed with remnants of necrotic epithelial cells (similar to respiratory distress syndrome of the newborn)



This figure shows the histologic appearance of the lung in a patient with ARDS.

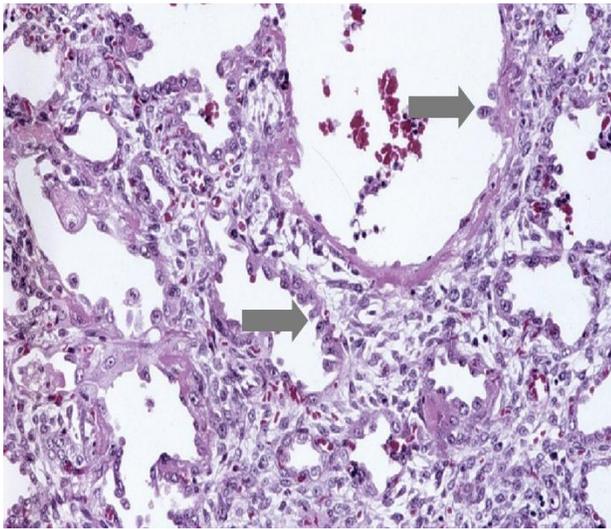
Some alveoli are collapsed while others are distended.

Many alveolar spaces are lined by bright pink hyaline membranes.

These changes represent the **diffuse alveolar damage** in the **acute phase**.

### In the organizing stage of ARDS :

- Proliferation of type II pneumocytes aiming to regenerate the alveolar lining.  
**Note** : resolution in such cases is unusual.
- More commonly , Intra-alveolar fibrosis due to organization of the fibrin-rich exudates.
- Marked thickening of the alveolar septa due to proliferation of interstitial cells and collagen deposition.



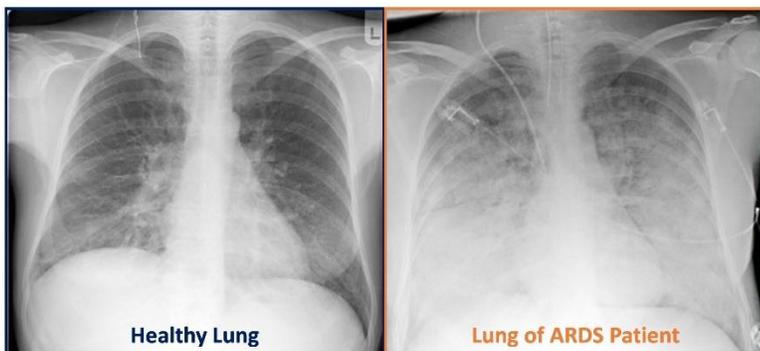
This figure shows the microscopic appearance of the healing stage.

This stage is marked by resorption of hyaline membranes , so they are inappreciable now.

Thickening of the alveolar septa by inflammatory cells , fibroblasts , and collagen.

The arrow points to the reactive type II pneumocytes.

### ➤ Radiographic findings of ARDS :



Radiographic findings:

X-ray shows bilateral opacities.

### ➤ Clinical features :

- Patients are hospitalized for one of the predisposing conditions
- Profound **dyspnea (shortness of breath)** and **tachypnea (increased respiratory rate)** 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 in some cases.**

➤ **OUTCOME:**

- 190,000 ARDS cases occur yearly in the US.
- In 85% of patients , the clinical syndrome of acute lung injury or ARDS develops within 72 hours of the initiating insult.
- Survival rate for ARDS vary depending on the age and the underlying cause , and presence of other associated illnesses.
- The overall hospital mortality rate is 38.5% .

Ranging from (mild – 27%) to (moderate – 32%) to (severe – 45%).

- Most patients who survive the acute insult recover normal respiratory function within 6 to 12 months, but the rest develop diffuse interstitial fibrosis leading to chronic respiratory insufficiency.

➤ **Predictors of poor prognosis of ARDS:**

- ✓ Advanced age.
- ✓ Bacteremia (sepsis).
- ✓ Development of multiorgan failure.

### Obstructive vs. Restrictive pulmonary diseases

**Diffuse pulmonary diseases** can be classified into two categories:

- ✓ **Obstructive airway diseases:** characterized by an increase in resistance to airflow caused by partial or complete obstruction at any level.

**Most important examples include:**

- 1) Emphysema
- 2) Chronic bronchitis
- 3) Bronchiectasis
- 4) Asthma

Expiratory obstruction may result either from :

- Anatomic airway narrowing, classically observed in asthma
- Or from loss of elastic recoil , characteristic of emphysema.

- ✓ **Restrictive diseases:** characterized by reduced expansion of lung parenchyma and decreased total lung capacity.

## Restrictive defects occur in two general conditions:

### 1) Chest wall disorders in the presence of normal lungs:

- Examples include : severe obesity, diseases of the pleura, and neuromuscular disorders that affect the respiratory muscles such as **Guillain–Barré syndrome (GBS)**.

### 2) Acute or chronic interstitial lung diseases:

- The classic acute restrictive disease is ARDS.
- Chronic restrictive diseases include the pneumoconiosis, interstitial fibrosis of unknown etiology, and infiltrative conditions such as sarcoidosis.

Case study (1) : 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**

Case study (2) : An 82-year-old woman is brought to the ER from a long-term care facility. 4 days ago, she aspirated her lunch, and the physician on call for the facility diagnosed her with **pneumonia**. During the past 24 hours, she has developed progressive dyspnea and restlessness. At times she is gasping for air. **Chest x-ray shows diffuse infiltrates.**

What is her diagnosis?

- A) Resorption atelectasis.    B) Restrictive lung disease.    **C) ARDS.**    D) chest tumor.