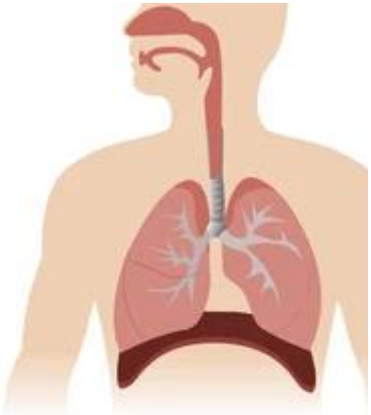
Respiratory System Module



Dr. Ola Abu Al Karsaneh

Upper Respiratory Tract Pathology

Nasopharyngeal Carcinoma

- Age: (15-25 & 60-69 yrs).

Etiology:

- Has strong links to **EBV,** and its genome is found in ~ ALL nasopharyngeal carcinoma

Clinical features

- Presents with upper cervical lymphadenopathy due to lymph node metastasis Or obstructive symptoms (nasal discharge or epistaxis).

Histologically:

1. Keratinizing squamous cell carcinoma.
2. Nonkeratinizing squamous cell carcinoma.
3. Undifferentiated carcinoma.

Undifferentiated carcinoma (lymphoepithelioma):

- The most common and the most closely linked with EBV.

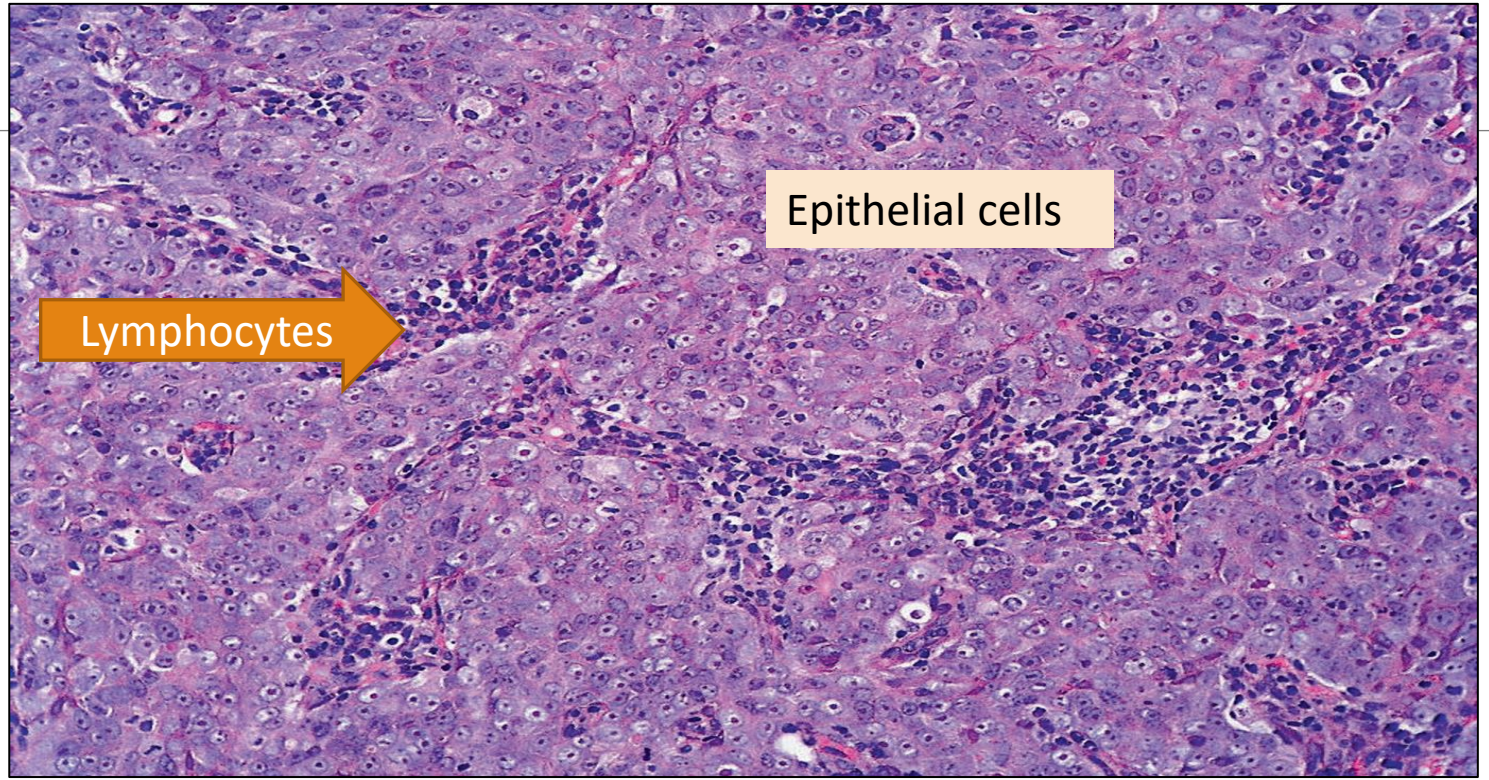
- Large epithelial cells with Indistinct cell borders (syncytial growth) and prominent eosinophilic nucleoli.

- Often with an influx of T lymphocytes.

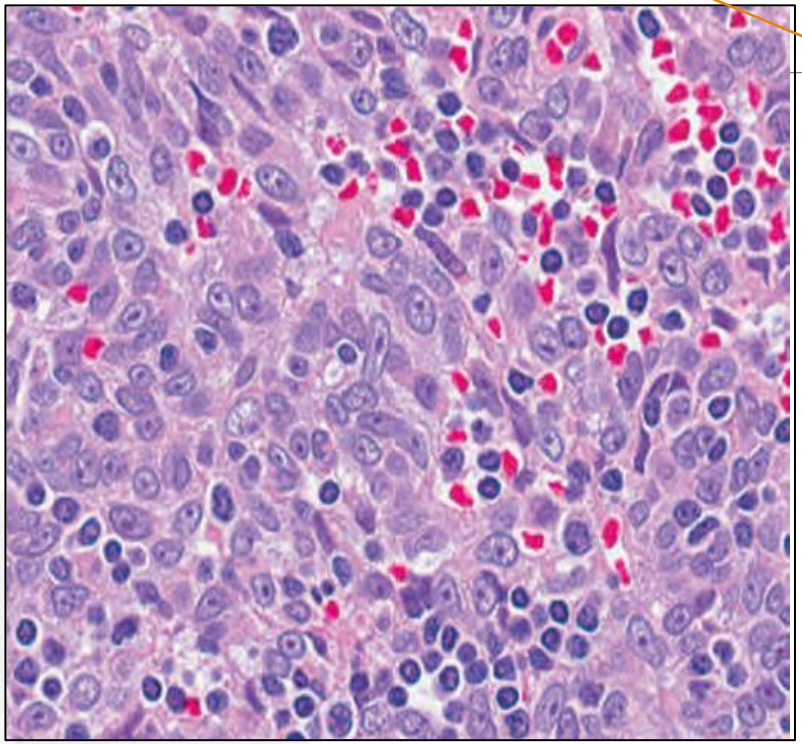
- EBV genomes can be detected in the serum or in tissue by in situ hybridization (ISH) or IHC

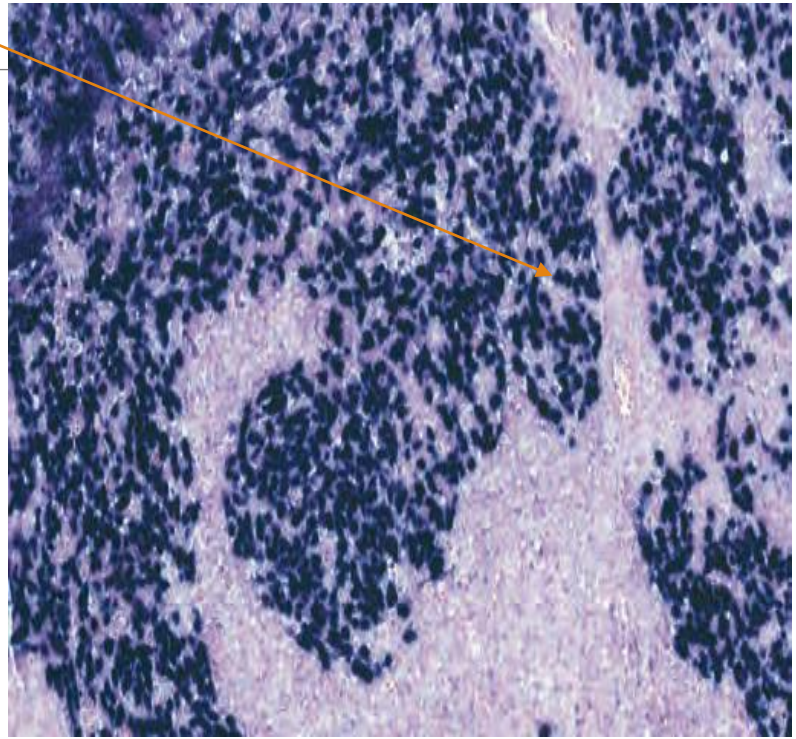
- It is the most radiosensitive, while the keratinizing SCC is the least radiosensitive

Undifferentiated carcinoma

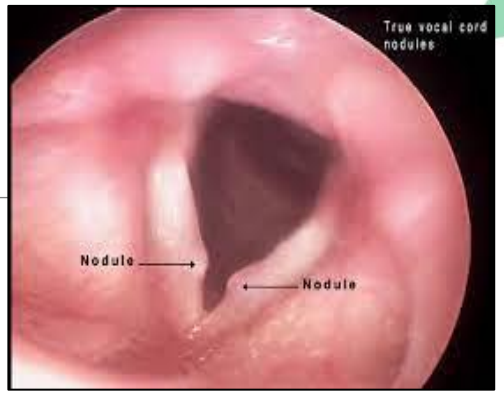


- The syncytium-like clusters of epithelium are surrounded by lymphocytes
- In situ hybridization for EBER-1 of EBV.





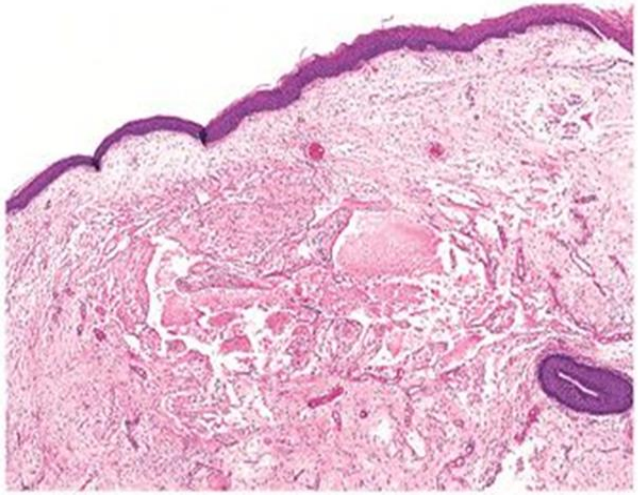
Vocal Cord Nodules and Polyps



- Usually on the true vocal cords, mostly in adults
- Occur chiefly in heavy smokers or singers (singer's nodes)

Histologically:

- Covered by squamous epithelium
- The core of the nodule is a loose myxoid connective tissue that may be variably fibrotic or have numerous vascular channels.
- **They virtually never give rise to cancers.**

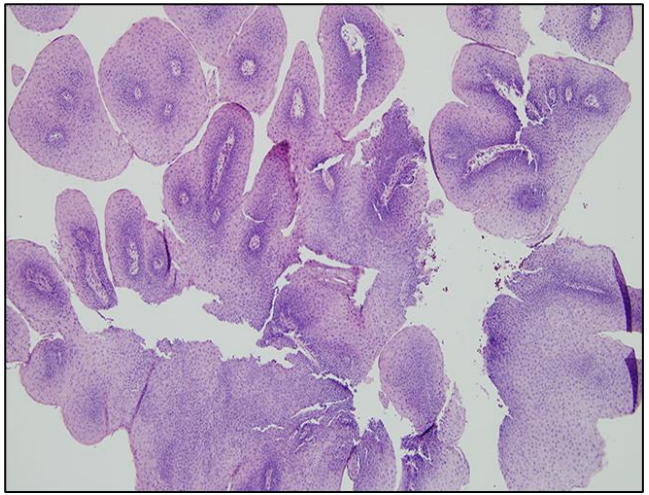


Laryngeal Papilloma Or Squamous Papilloma

- Usually located on the **true vocal cords** as a soft excrescence.
- Single in adults but often multiple in children and recur after removal
- Caused by HPV types 6 and 11.
- **Cancerous transformation is rare.**

Histologically:

-Multiple fingerlike projections with central fibrovascular cores and covered by stratified squamous epithelium.



Carcinoma Of The Larynx:

- Mostly in 6th decade.

- M>F (7: 1).

- Present as persistent hoarseness, dysphagia, and dysphonia.

-Nearly all cases occur in smokers, and alcohol and Asbestos exposure also may play a role.

- **HPV** sequences detected in ~ **15%** of tumors (**better prognosis**).

- The tumor develops directly on:

- The vocal cords (**glottic tumors**) **most common**, or
- Above the cords (supraglottic) or
- Below the cords (subglottic).

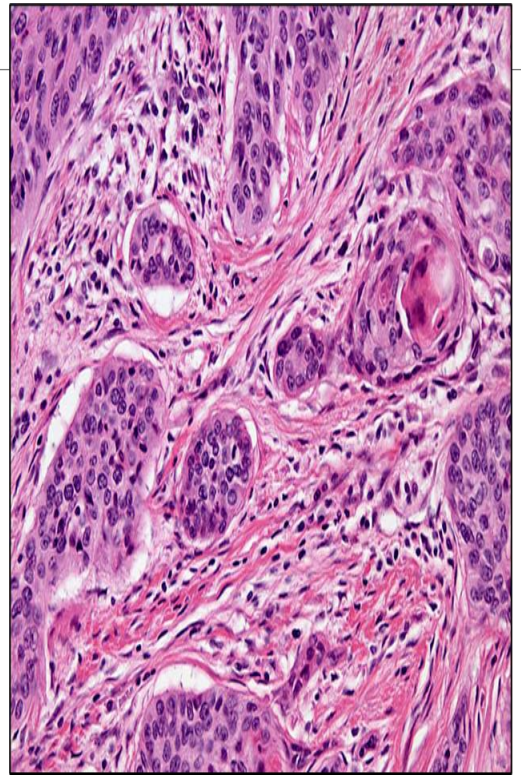
-**Grossly:** vary from white or reddened thickenings to irregular verrucous or ulcerated lesions.

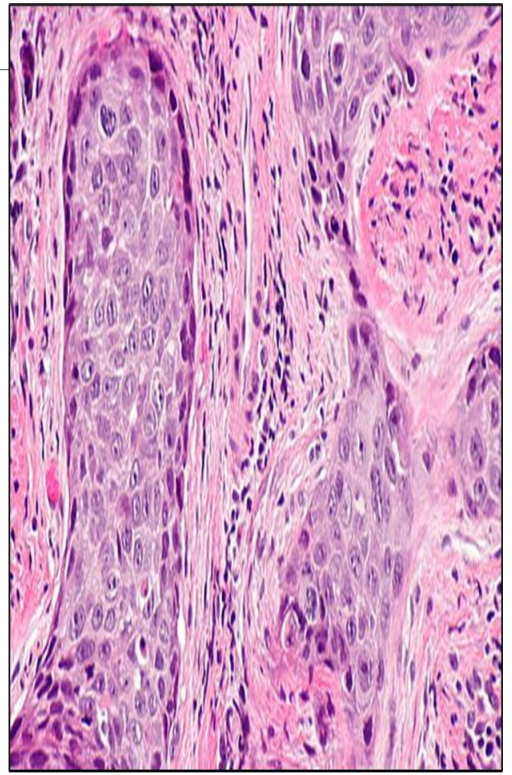
- The likelihood of the development of carcinoma is directly proportional to the grade of dysplasia when the lesion is first seen.

Histologically:

- About 95% are typical **squamous cell carcinomas.**

- Rarely, adenocarcinomas are seen.





Prognosis (depends on the location):

- About 90% of **glottic tumors** are **confined to the larynx** at diagnosis.

- About one-third of **supraglottic** tumors **metastasize to regional (cervical) lymph nodes.**

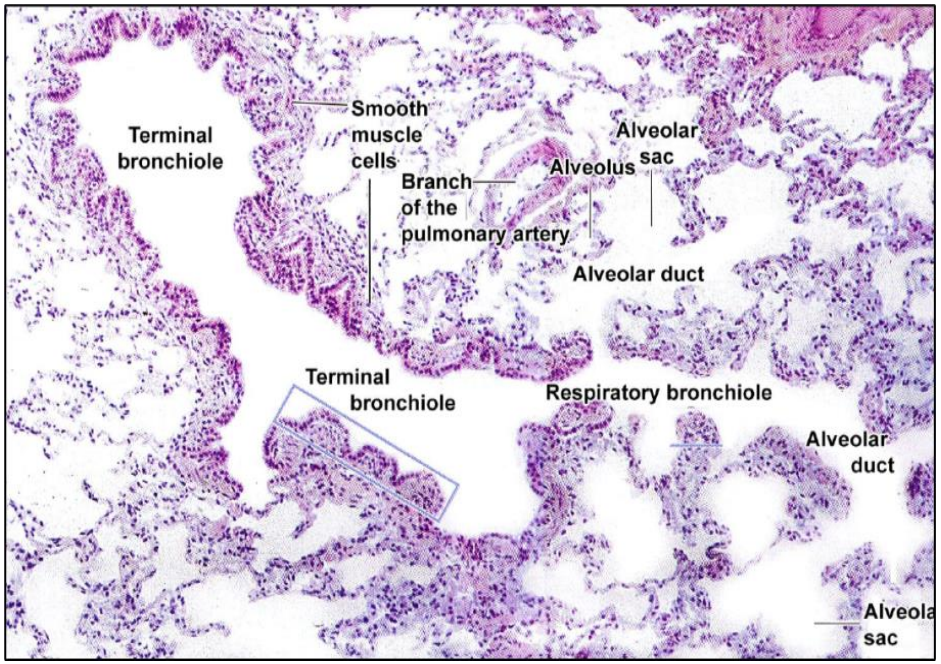
- The **subglottic** tumors tend to remain clinically quiescent and usually present as **advanced disease.**

-With treatment, many patients can be cured, but about one-third die of the disease (due to metastases and cachexia).

Lower Respiratory Tract Pathology

- The pulmonary **acini** are composed of **respiratory bronchioles** that proceed into **alveolar ducts,** which branch into the **alveolar sac** **(**formed of **alveoli)**

-A cluster of 3-5 terminal bronchioles, each with its acinus, is called a **lobule.**



The alveolar walls (or alveolar septa) consist of the following components:

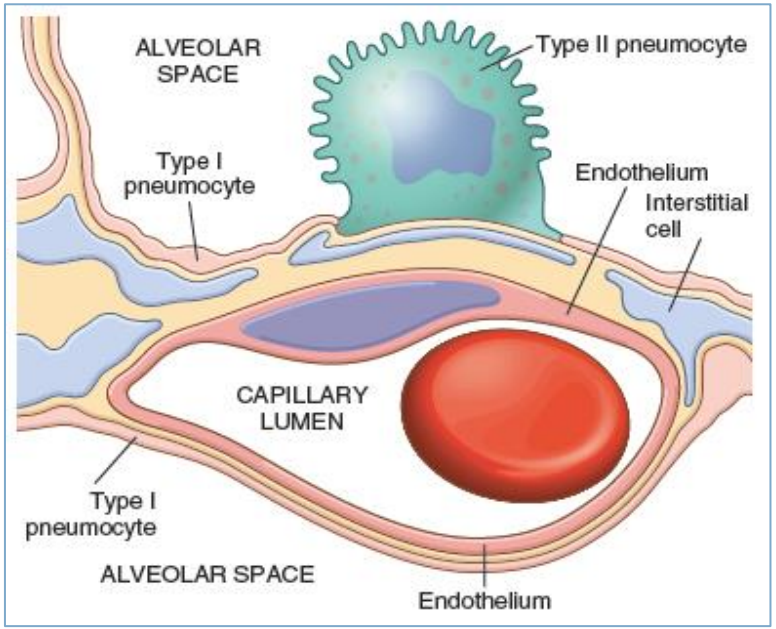
1. The capillary endothelium and basement membrane.

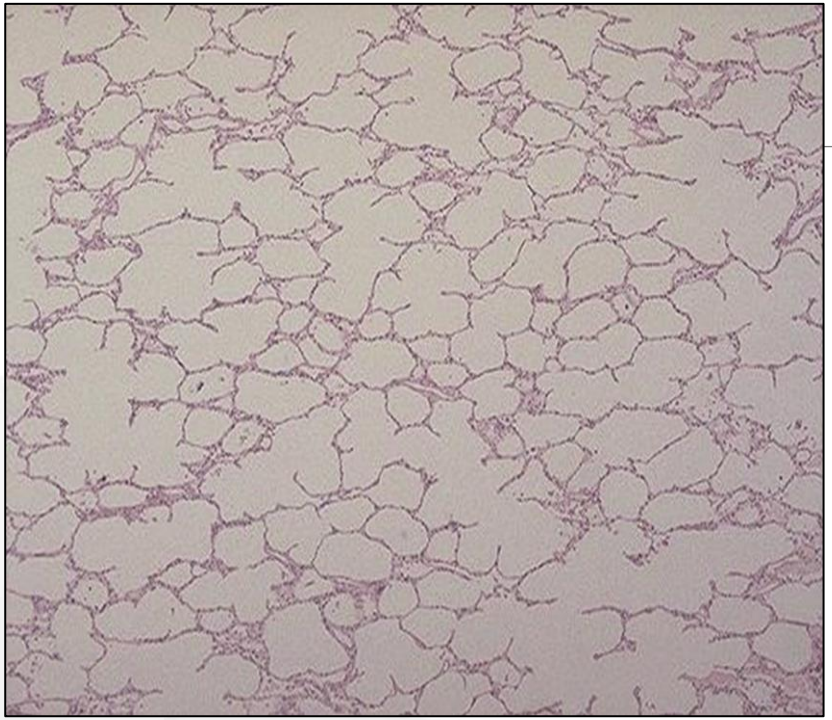
2. The pulmonary interstitium

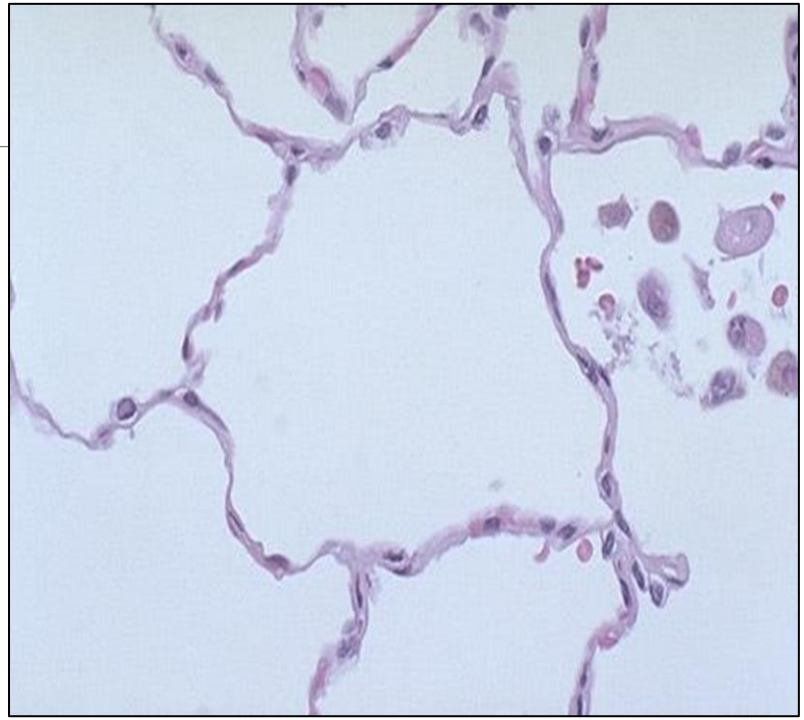
3. Alveolar epithelium

- A flattened plate-like Type I pneumocytes.

- Rounded Type II pneumocytes(source of pulmonary surfactant and involved in the repair of pulmonary epithelium).







Atelectasis (COLLAPSE)

- **Loss of lung volume caused by inadequate expansion of air spaces.**
- It results in the shunting of inadequately oxygenated blood from pulmonary arteries into veins, **leading to a ventilation-perfusion imbalance and hypoxia.**

Outcomes depend on:

1- Cause.

2- Size of involved area.

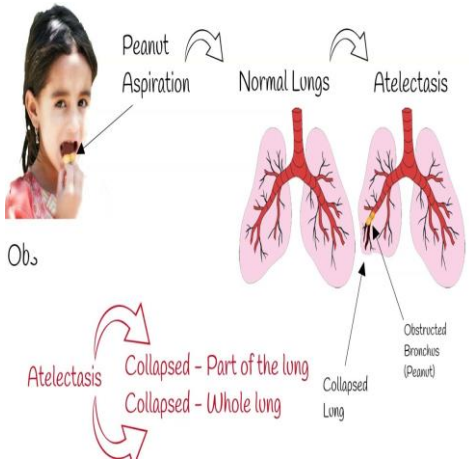
3- Duration to start treatment.

Atelectasis (except when caused by contraction) is potentially **reversible**

Types of Atelectasis :

I- Resorption atelectasis :

- Occurs when **obstruction** prevents air from reaching distal airways.
- The air already present becomes absorbed & alveolar collapse follows.
- An entire lung, a lobe, or one or more segments may be involved.
- The most common cause of bronchial obstruction is mucus or mucopurulent plug or aspiration of foreign bodies and tumors.



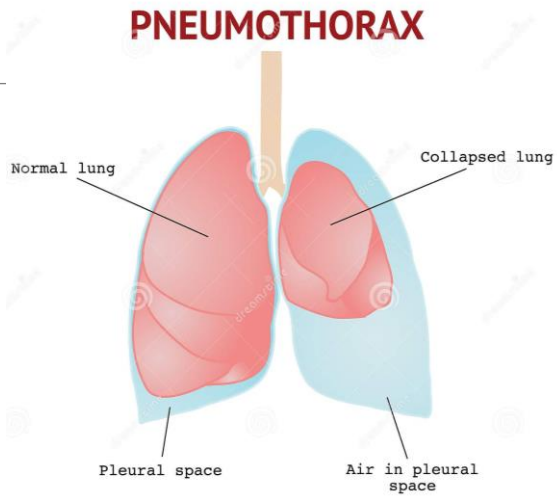
Mediastinal Shift to Same Side

II- Compression atelectasis :

- Sometimes called **passive** or **relaxation, atelectasis** is usually associated with the accumulation of fluid, blood, or air within the pleural cavity, which collapses the adjacent lung.

- This frequently occurs with **pleural effusion** and **pneumothorax.**

- Maybe caused by an elevated diaphragm.



Mediastinal Shift to Opposite Side

III- Contraction atelectasis :

- Or **cicatrization** atelectasis occurs when local or generalized **fibrotic changes** affecting the lung or pleura hamper lung expansion.

- Usually, **irreversible.**

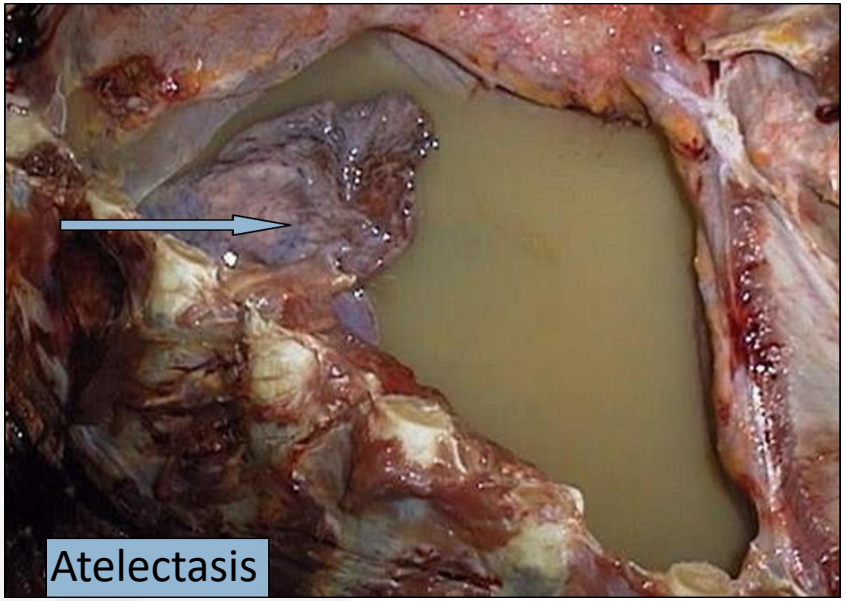
IV- Microatelectasis:

- Due to loss of surfactant.

Morphology of Atelectasis :

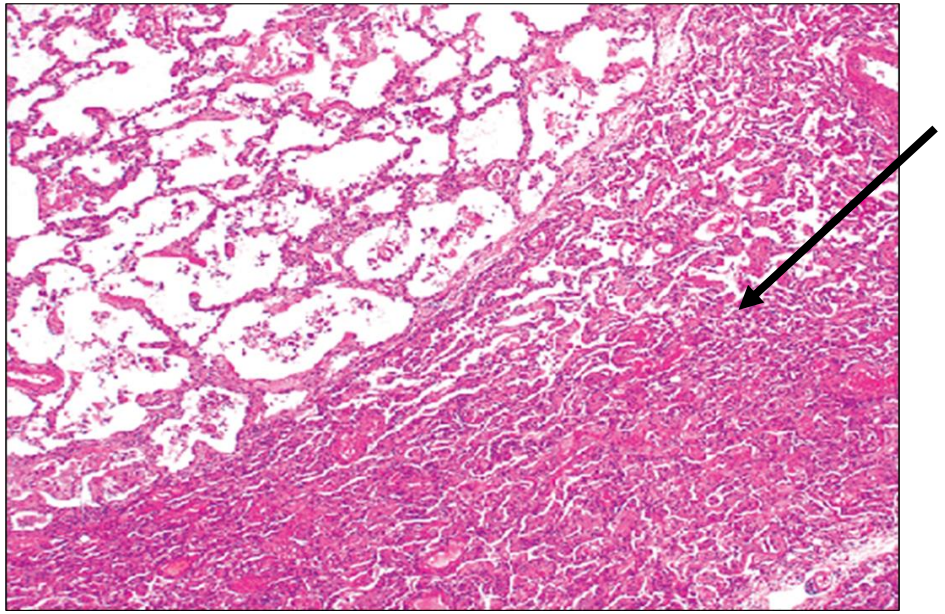
Gross:

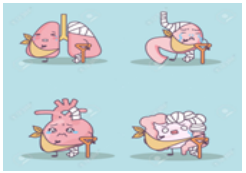
- Shrunken lung.



Microscopic:

-Slit-like alveoli, congested septae.





Acute Respiratory distress syndrome (ARDS):

- A severe form of acute lung injury.
- Clinical syndrome that is caused by many conditions.
- Characterized clinically by:
    - Sudden and Acute onset of severe dyspnea.
    - Severe arterial hypoxemia, hypercapnia and cyanosis

      ** This will lead to severe life- threatening respiratory insufficiency

Radiology : Diffuse bilateral alveolar infiltrate (GGO).

Histologically: known as *diffuse alveolar damage* ***(DAD).***

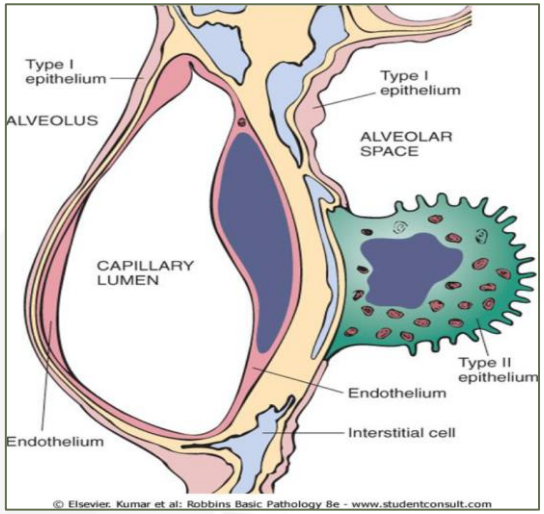
- **The above-mentioned manifestations should happen in the absence of left-sided heart failure.**

Etiology:

Sepsis & pneumonia account for 40-50% of cases

Direct lung injury	Indirect lung injury
Common causes	
Pneumonias	***Sepsis***
Aspiration of gastric content	***Severe trauma with shock*** Multiple bone fractures, Head trauma, Severe Burns
Uncommon causes	
Pulmonary contusion.	**Cardio-pulmonary bypass.**
Fat embolism	**Acute pancreatitis**
Inhalation injury	**Transfusion of blood products**

Pathogenesis:



-The integrity of the **alveolar-capillary membrane** is compromised either by **endothelial or epithelial** injury or both.

- This leads to increased vascular permeability, alveolar edema, loss of diffusion capacity & surfactant abnormalities due to damage of type II pneumocytes.

Early after **injury** ➡ increased synthesis of

IL 8 by pulmonary **macrophages**.

- IL-8 is a **neutrophil** chemotactic & activating agent .

- **Neutrophils** have an important role in pathogenesis of ARDS .

Release oxidants protease, platelets activating factor and leukotrienes

Cause damage to alveolar epithelium and endothelium & maintain the inflammatory cascade

- The destruction is opposed by endogenous antiproteases, anti-oxidants & anti-inflammatory cytokines.

- The balance between the destructive (*pro-inflammatory)* & the protective (*anti-inflammatory)* factors that determine the clinical severity and the degree of tissue injury of ARDS.

Later:

- Macrophage-derived fibrogenic factors (e.g **TGF**) ⟹ **Recruitment of fibroblast → Fibrogenesis.**

Morphology (phases of ARDS):

- Acute/Exudative phase:

- The lungs are red, firm, airless, and heavy.

Microscopically:

- There is capillary congestion.

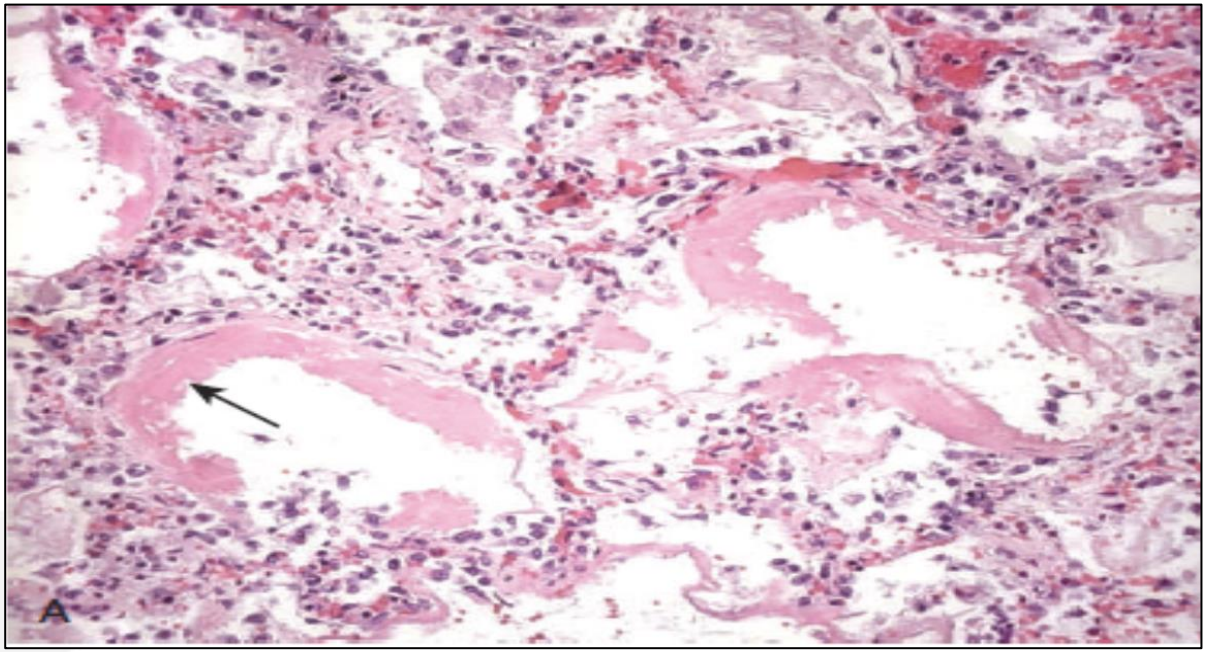
- Interstitial and intraalveolar edema & hemorrhage, and collection of neutrophils in capillaries.

- Necrosis of alveolar epithelial cells

- Collapse of alveolar parenchyma

- The **most characteristic** finding is the presence of **hyaline membrane** lining the distended alveolar ducts.

Acute phase. Some alveoli are collapsed, while others are distended; many are lined by right pink hyaline membranes (arrow).



Organizing/ proliferative phase:

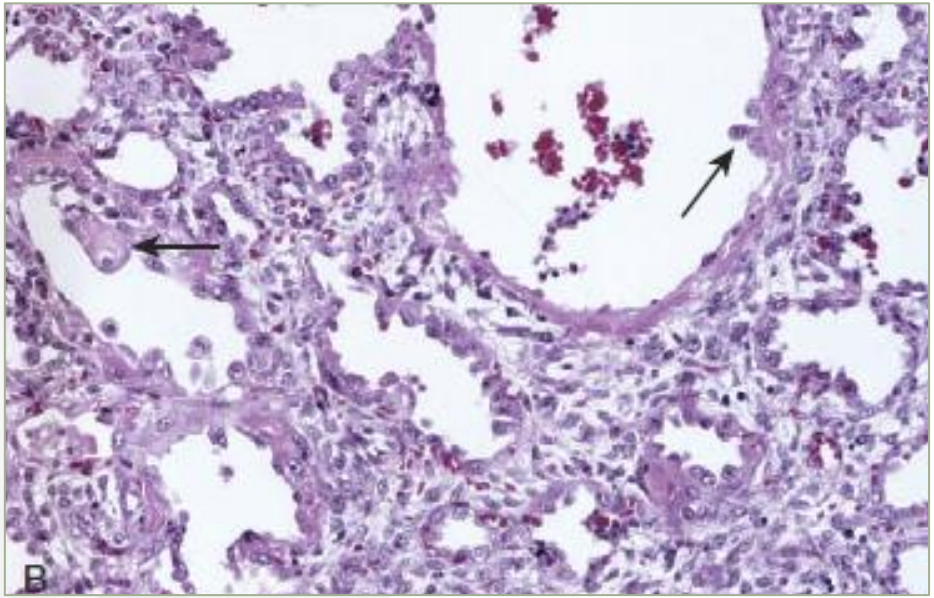
-Marked proliferation of reactive **type II pneumocytes** trying to regenerate the alveolar lining.

- Resolution is unusual; more commonly, there is an organization of the fibrin exudates with resulting **intra-alveolar fibrosis (organizing pneumonia (OP)).**

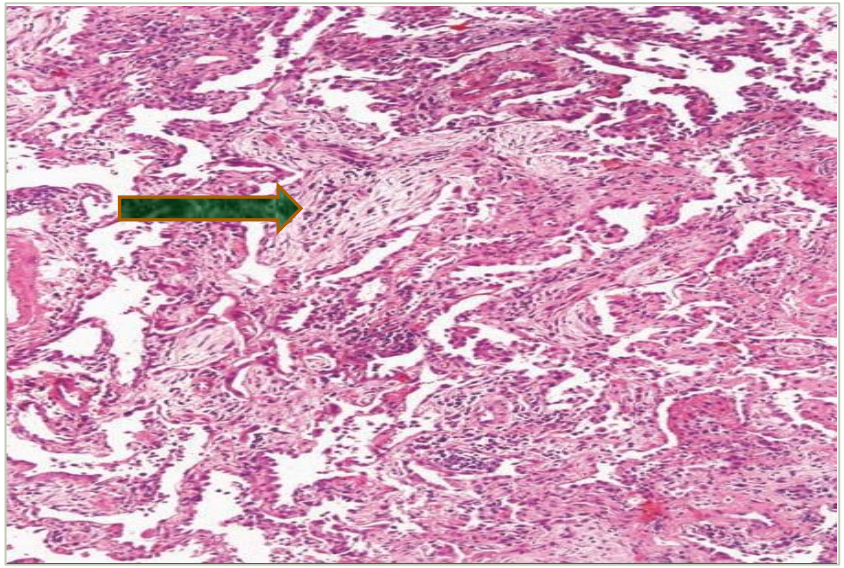
- Marked thickening of alveolar septa caused by the proliferation of interstitial cells & deposition of collagen.

Fibrotic phase: Usually, after several weeks on a respirator.

Thickening of alveolar septa by inflammatory cells, fibroblasts, and collagen. Numerous reactive type II pneumocytes are also seen (arrows), associated with regeneration and repair.



Organizing DAD with **granulation tissue plugs in alveolar ducts (OP).**

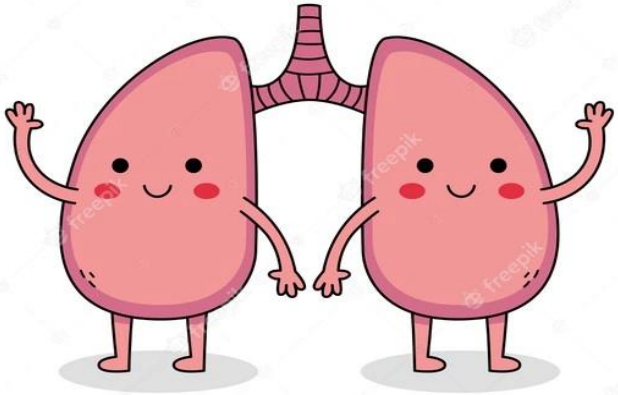


Clinical course :

- 85% of patients develop the clinical symptoms within 72 hours of the initiating insult.

-The predicting factors in ARDS are:

- Age.
- Underlying bacteremia or sepsis.
- Development of underlying system failure as cardiac, renal or hepatic (multiorgan failure).



Thank You