

# Respiratory System Module

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**Dr. Ola Abu Al Karsaneh**

## Nasopharyngeal Carcinoma → malignant epithelium tumor

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

### Etiology:

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

### Clinical features

ممکن یجی المرضی clinically على شكل

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

### Histologically:

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



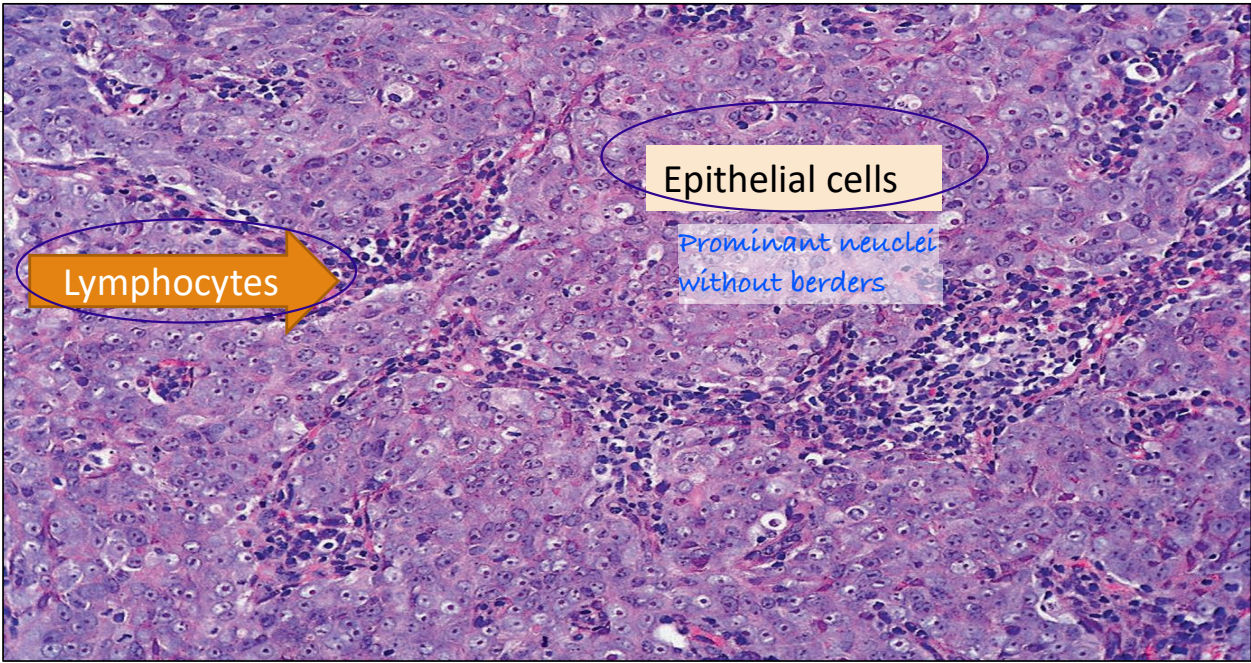
بكون ال differentiation قليل جدا و هو يلي رح نحكي عنه briefly و اله اسم تاني يلي هو ال lymphoepithelioma

ليش اسمه lymphoepithelioma ، لانه مكون من large epithelial cell وهاي الخلايا بتتميز انه cell border واضحين لهيك هي indistinct cell border

## 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.  
ببينوا ال Nuclei كلهم كأنهم موجودين بنفس السيتوبلازم بدون cell border
- Often with an influx of T lymphocytes. → عشان هيلك lympho
- EBV genomes can be detected in the serum or in tissue by in situ hybridization (ISH) or IHC  
Immunohistochemistry ↓
- It is the most radiosensitive, while the keratinizing SCC is the least radiosensitive

**Undifferentiated carcinoma**



Lymphocytes

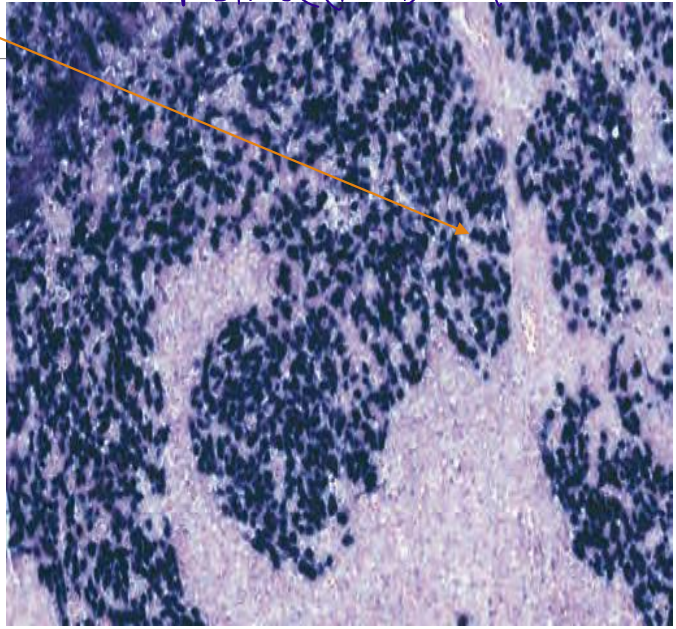
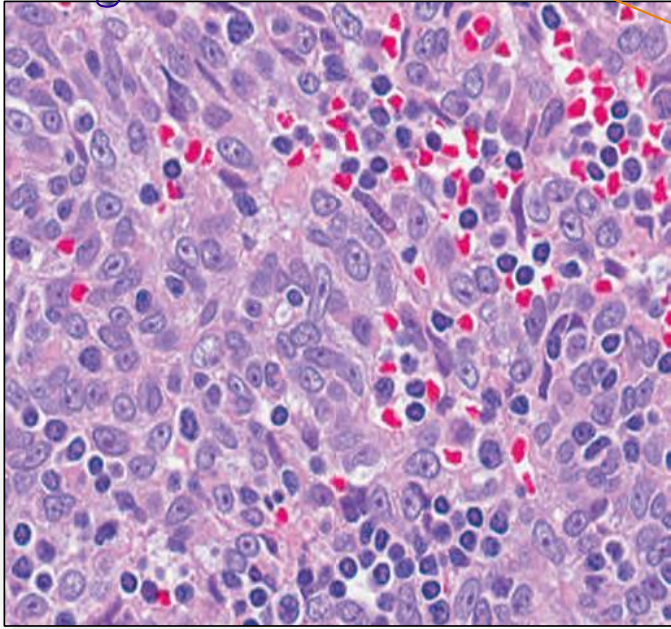
Epithelial cells

Prominant nuclei  
without berders

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

(syncytial growth)  
↙

Positive (ISH) (EBV)



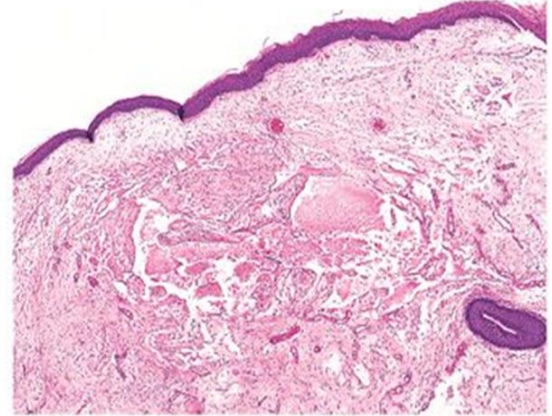
## Vocal Cord Nodules and Polyps

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

يعني بتصير عند الناس يلي  
Irritation ممكن يصير عندهم  
vocal cord due to smoking  
or over use

**Histologically:** *founded nodule*

- 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.** *benign tumor*



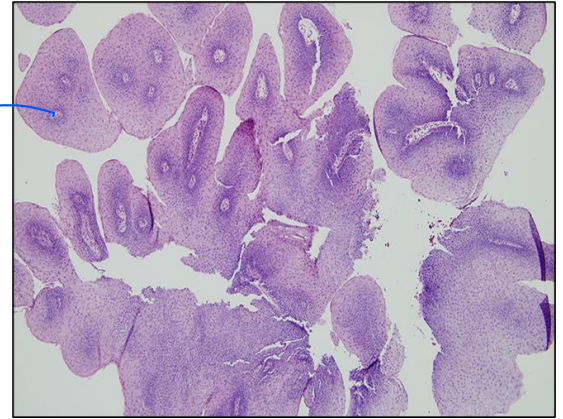


## Laryngeal Papilloma Or Squamous Papilloma

- 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. (low risk type)
- **Cancerous transformation is rare.** نادراً ما تتحول الى cancer

### Histologically:

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



3.

## Carcinoma Of The Larynx:

النهم

- Mostly in 6<sup>th</sup> decade.

male > Female

- M>F (7: 1).

بحة في الصوت

صعوبة بلع

خلل في النطق

- 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).

عدد قليل .

في نسبة قليلة من الحالات ممكن تكون مرتبطة بال HPV virus . و بهاي الحالة يكون الها better prognosis

- The tumor develops directly on:

• The vocal cords (glottic tumors) most common, or

• Above the cords (supraglottic) or مركزا و بيت أكثر اشياء

• Below the cords (subglottic).



مش شرط إنه شخص السرطان مباشرة وهو *invasive* , أحيانا ممكن نقدر نشخص المريض بالمراحل الأولى لما يكون عنده *dysplasia* , وساعتها احتمالية انه يصير عنده *invasive carcinoma* بنعتمد على درجة ال *dysplasia* , كل ما كانت *sever* اكثر كلما زاد خطر انه يكون عنده *invasive carcinoma* اكثر

keratin & intercellular bridges  
= SCC

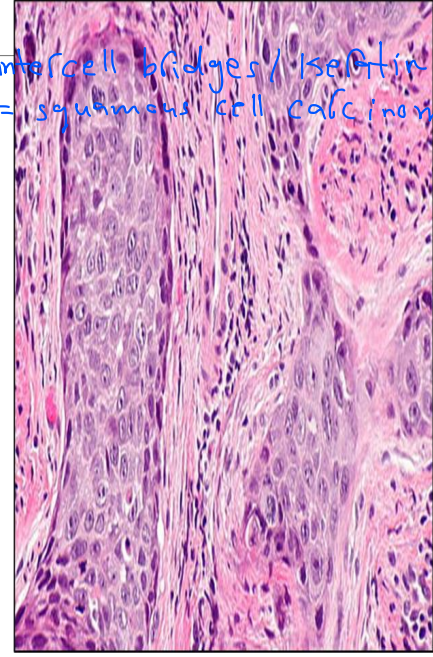
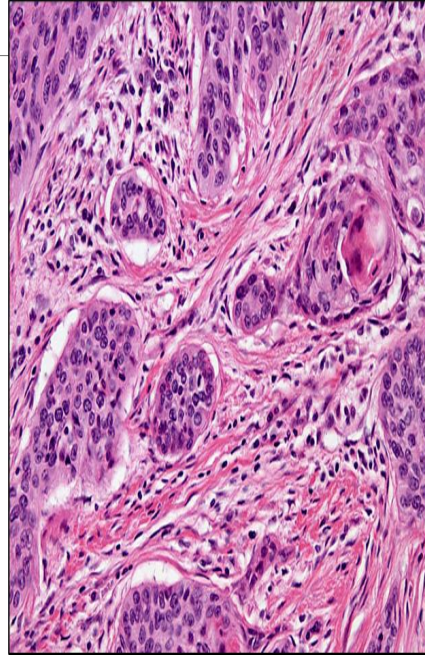
-Grossly: vary from white or reddened thickenings to irregular verrucous or ulcerated lesions.

- 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.



intercell bridges / keratin  
= squamous cell carcinoma

## ○ Prognosis (depends on the location):

- About 90% of **glottic tumors** are **confined to the larynx** at diagnosis. ← بظلم موجوده فيك روا بتنتش
- About **one-third** of **supraglottic** tumors **metastasize to regional (cervical) lymph nodes**. لئنه فيها lymphatic أكثر
- The **subglottic** tumors tend to remain clinically quiescent and usually present as **advanced disease**. يعني ما بيعطوا manifestation on the patient  
عشان هيك احنا بنطول لحتى نكتشفه  
↓  
تحت ال  
Vocal cord
- With treatment, many patients can be cured, but about one-third die of the disease (due to metastases and cachexia).

هيك بنكون خلاصنا ال upper.  
respiratory tract pathology

# Lower Respiratory Tract Pathology

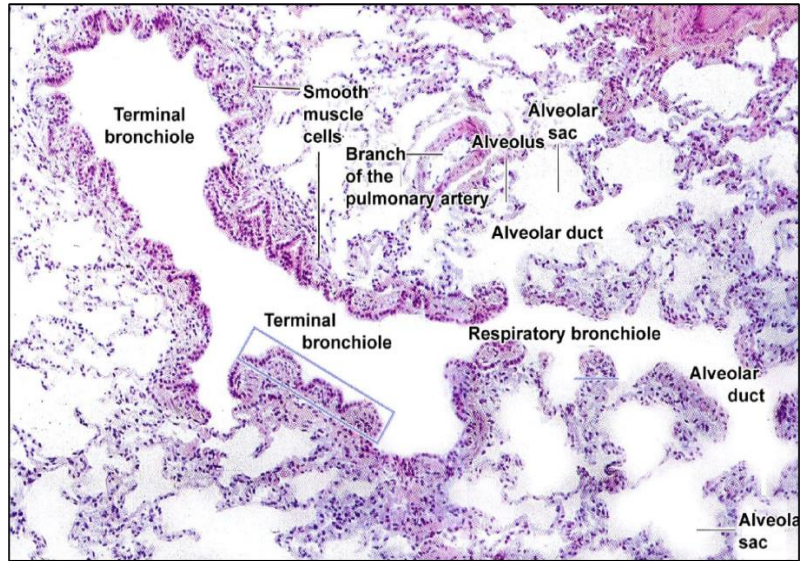
تحكي سوّج أُناتوم

هاد ال structure يلي بعد  
ال terminal bronchiole

- The pulmonary **acini** are composed of **respiratory bronchioles** that proceed into **alveolar ducts**, which branch into the **alveolar sac** (formed of **alveoli**) 1./2./3. → parts of acini

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

\* acini is distal to terminal bronchiole





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

١. يبعثوننا ال surfactant material اللي بتمنع ال collapse و بتخلي ال alveolus فاتحة .

٢. بتساعد بال repair لو صار في injury بال epithelial cell in alveoli

1. The capillary endothelium and basement membrane.

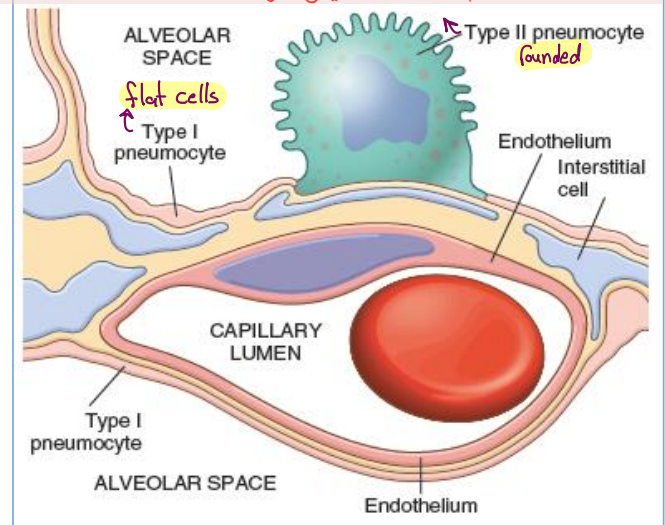
2. The pulmonary interstitium

3. Alveolar epithelium

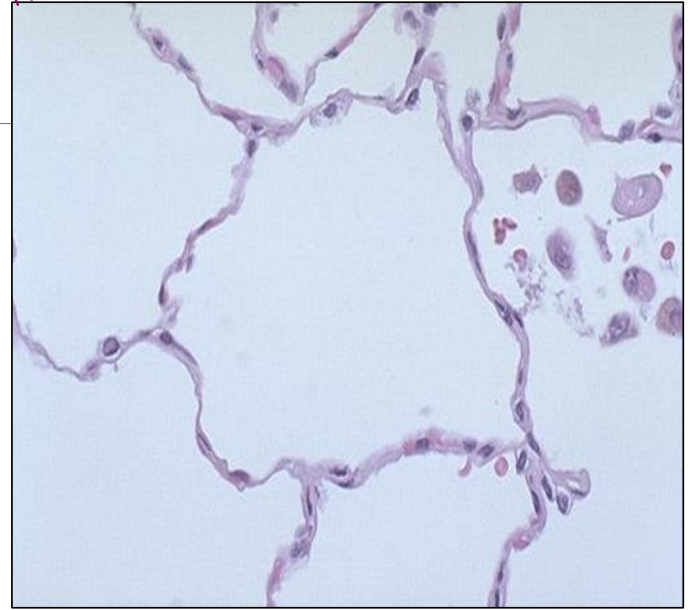
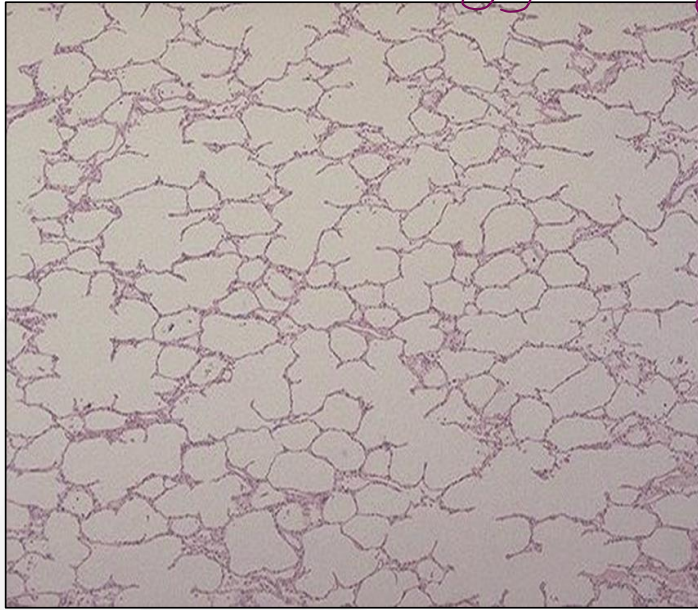
inflammatory cell, بنشوف فيها  
fibroblast, بتكون very thin

- A flattened plate-like Type I pneumocytes.

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



☆ normal histology of lung parenchyma (alveoli)



general pattern ← كثير مهمين للأنف  
يمكن نستوفهم مع أكثره مرض

1.

## 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.**

رح يصير مشكلة في تبادل  
الغازات

Outcomes depend on:

- 1- Cause.
- 2- Size of involved area.
- 3- Duration to start treatment.

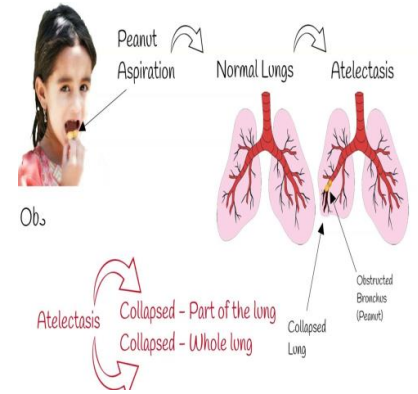
Atelectasis (except when caused by contraction)  
is potentially **reversible**

كلمة reversible طاعة ال

# Types of Atelectasis :

## I- Resorption atelectasis :

- Occurs when **obstruction** prevents air from reaching distal airways. طيب شو سبب هاد التسكير؟ ممكن تجمع mucos او tumor او aspiration foreign material يسد مجرى التنفس و القصبات
- 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 **muco-purulent plug** or **aspiration of foreign bodies** and **tumors**.

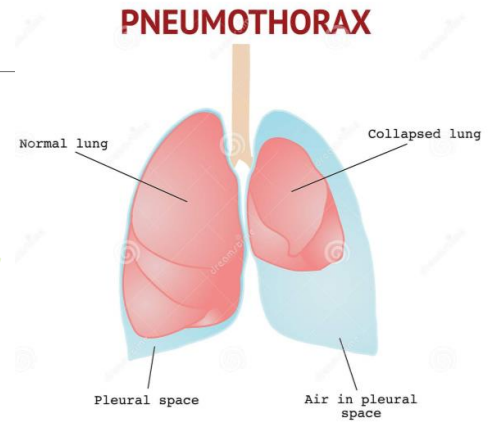


**Mediastinal Shift to Same Side**

الـveoli  
بعض في اسفء بـفـf

## 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.** ← هو النوع الوحيد

### IV- Microatelectasis:

- Due to loss of surfactant.

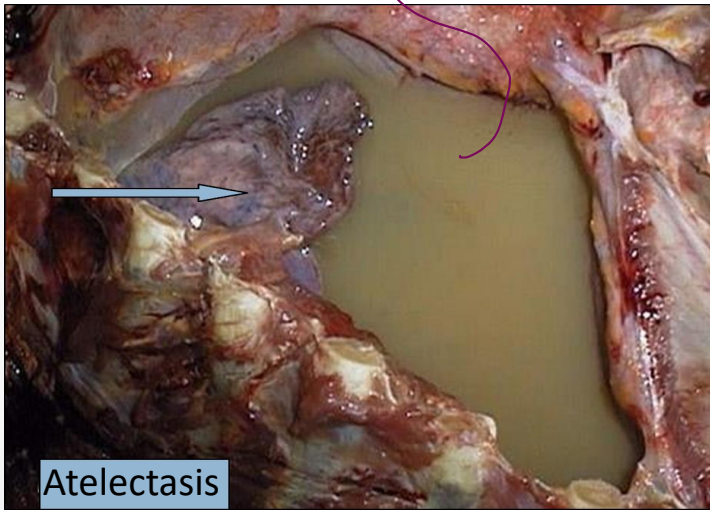
منطقة ضعف سطحها  
↓  
Collapsed

# Morphology of Atelectasis :

## Gross:

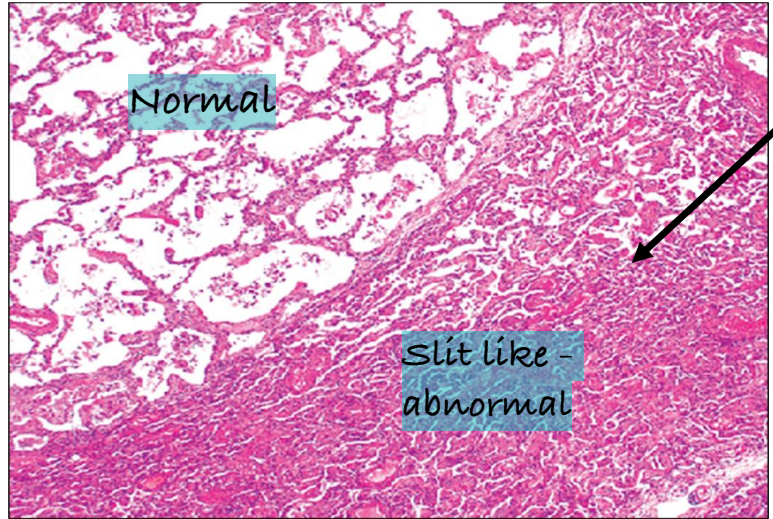
- Shrunken lung.

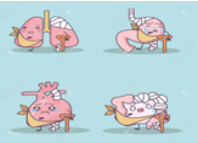
→ fluid



## 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 <sup>high level of CO<sub>2</sub></sup>
- \*\* This will lead to severe life-threatening respiratory insufficiency

**Radiology** : Diffuse bilateral alveolar infiltrate (GGO).

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

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

يعني لو صار عند المريض <sup>سريع</sup> acute shortness of breath فجأة صار عنده ضيق نفس و hypoxia and hypercapnia ، وهو عنده ARDS ، heart failure

# Etiology: Causes

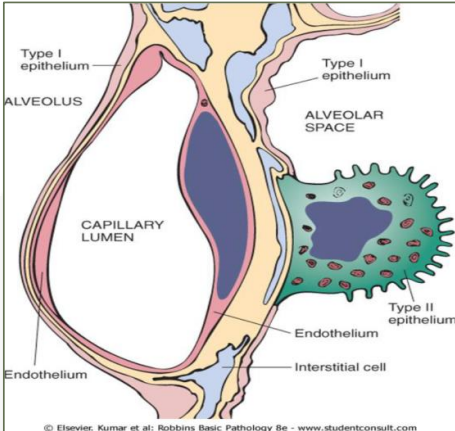
Sepsis & pneumonia  
account for 40-50% of  
cases

ما حكت عنهم الدكتور

Direct lung injury	Indirect lung injury
<b>Common causes</b>	
<b>Pneumonias</b> infection in lung	<b>Sepsis</b>
<b>Aspiration of gastric content</b> واحد شربة (تشدق) وطلعت محتويات المعدة راحة لل lung، بتمل injury	<b>Severe trauma with shock</b> Multiple bone fractures, Head trauma, Severe Burns
<b>Uncommon causes</b>	
<b>Pulmonary contusion.</b>	<b>Cardio-pulmonary bypass.</b>
<b>Fat embolism</b>	<b>Acute pancreatitis</b>
<b>Inhalation injury</b>	<b>Transfusion of blood products</b>

# Pathogenesis:

alveolar wall/septum دیباہ آئیں گے



-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 .

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graph TD; A["- Neutrophils have an important role in pathogenesis of ARDS ."] --> B["Release oxidants protease, platelets activating factor and leukotrienes"]; B --> C["Cause damage to alveolar epithelium and endothelium & maintain the inflammatory cascade"]; style A stroke:#000,stroke-width:1px; style B stroke:#000,stroke-width:1px; style C stroke:#000,stroke-width:1px;
```

Release oxidants protease, platelets activating factor and leukotrienes

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

أکید الجسم بده يحاول يقاوم



- 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.

neutrophil و بتعمل inflammation

وال inflammation and inflammatory mediators بتعمل

بعدين بصير healing ، distraction in the Alveolar wall

على شكل fibrosis, and fibrogenesis process

## 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 due to loss of surfactant

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

أحنا حكينا بال pathogenesis انها بتصير بسبب loss the

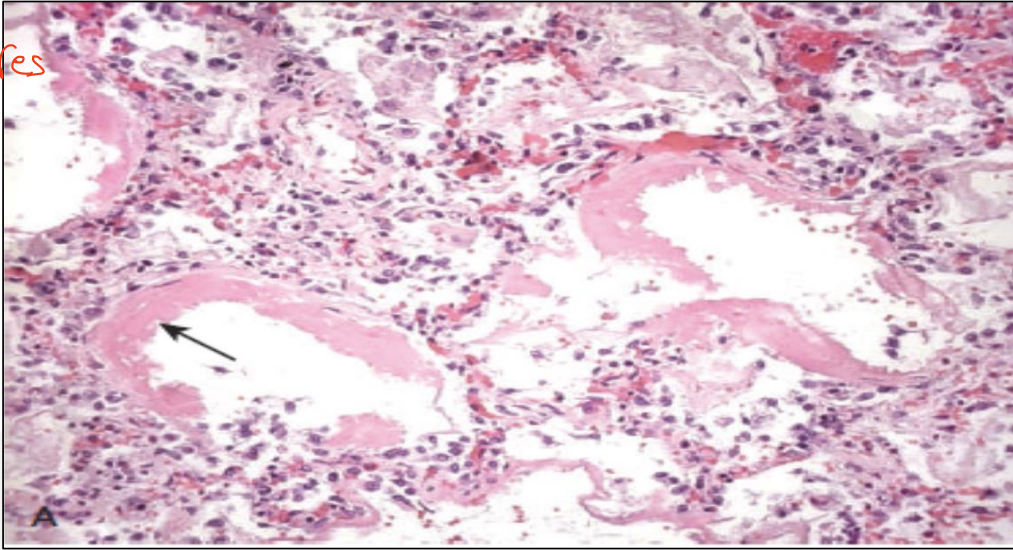
يعني بصير عنا ، integrity of alveolar wall or alveolar septum  
و هاد فعليا يلي ، alveolar and endothelial cells لل destruction

روح نشوفه بال يعني بال morphology biopsy



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

The main features  
of Acute  
phase



كيف بدو بصير ال healing ؟

بصير عنا proliferation  
لشغلين : pneumocyte type 2  
And Prolifration of fibroblast

بصير في organizing hyaline  
و بصير يتحول membrane  
fibrosis

## 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 **hyaline membrane** (بطل عنا) with resulting **intra-alveolar fibrosis (organizing pneumonia (OP))**.

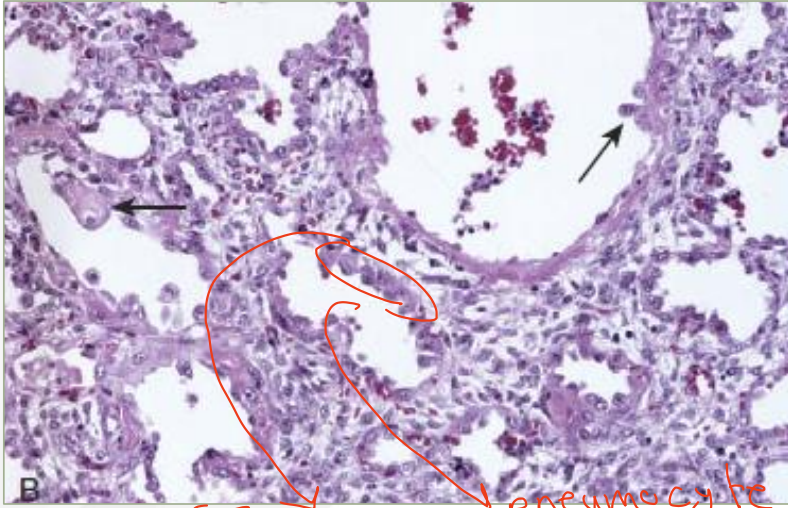
- Marked thickening of alveolar septa caused by the proliferation of interstitial cells & deposition of collagen.

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

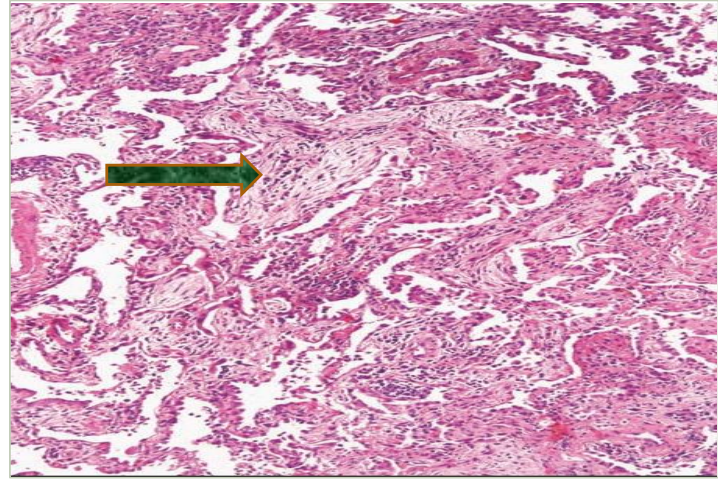
The main features of organizing phase → proliferation of pneumocyte II

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)**. → organizing pneumonia



Thick III pneumocyte type II



alveoli or ال هاد بنشوفه جوا  
alveolar duct

# Clinical course :

→ high mortality

- 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).

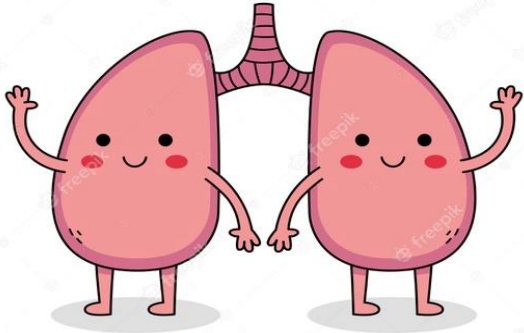
تو کی بچد؟



Bad outcome

→ poor outcome





Thank You

Done by Sadeel Alfaqeer