وَقُل رَّبِّ زِدْنِي عِلْمًا

# RESPIRATORY SYSTEM

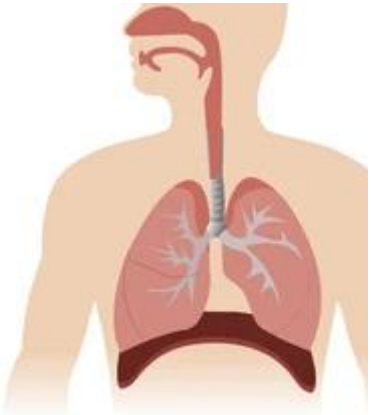
## HAYAT BATCH

SUBJECT : Pathology

LEC NO. : 1

DONE BY : Dana khalaf

# Respiratory System Module



Dr. Ola Abu Al Karsaneh

# Upper Respiratory Tract Pathology

Malignant tumour

## 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):

بسبب وجود T lymphocyte

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

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

الأنوية بتبين موجودة بنفس السيتوبلازم(زي كأنهم مندمجين )بدون cell borders

- Often with an influx of T lymphocytes.

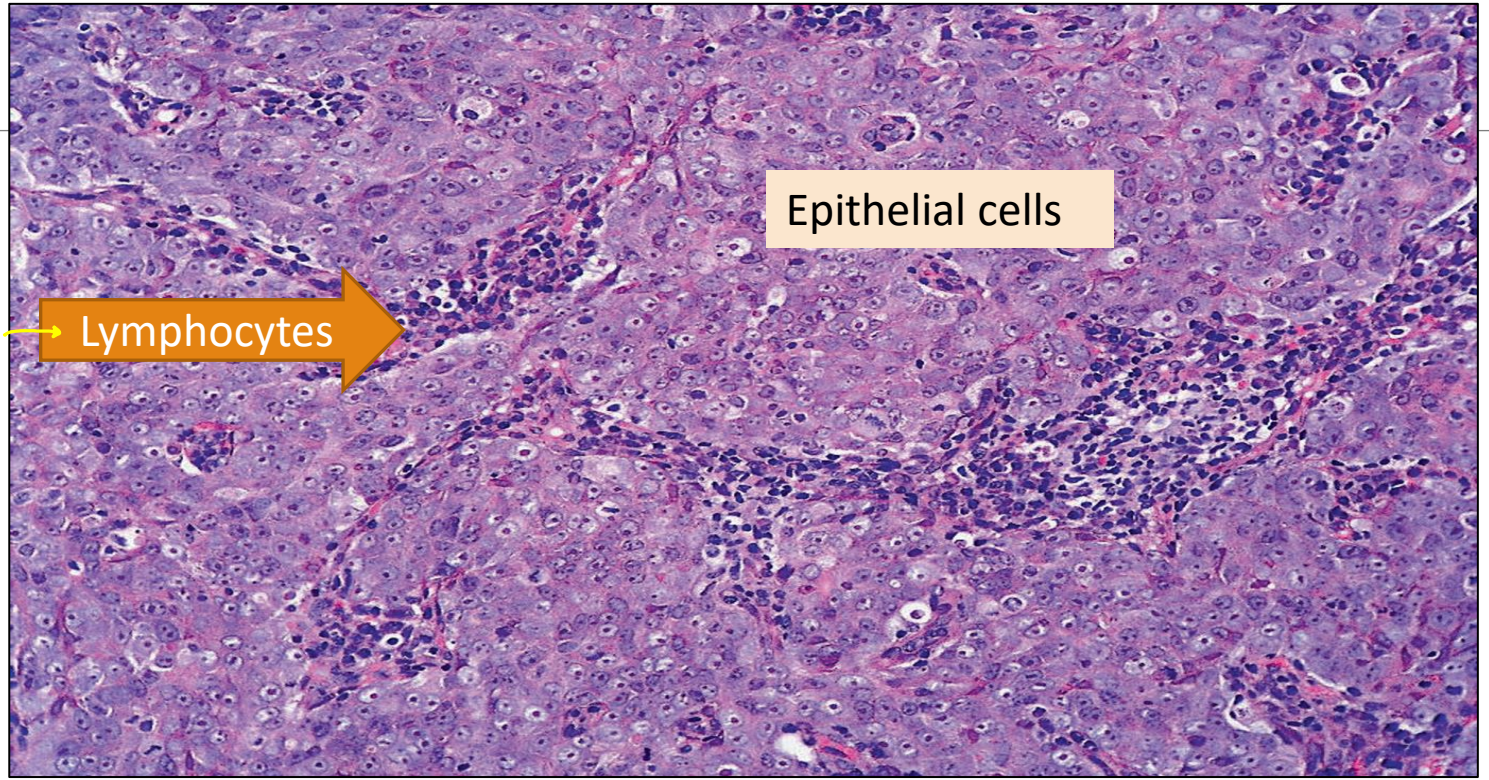
الصبغة بتكون +لل EBV

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

*الأكثر استجابة
- It is the most radiosensitive, while the keratinizing SCC is the least radiosensitive

Sheets of epithelial cells الهم prominent nucleoli (pink)
لكن مافي borders (syncytial growth)

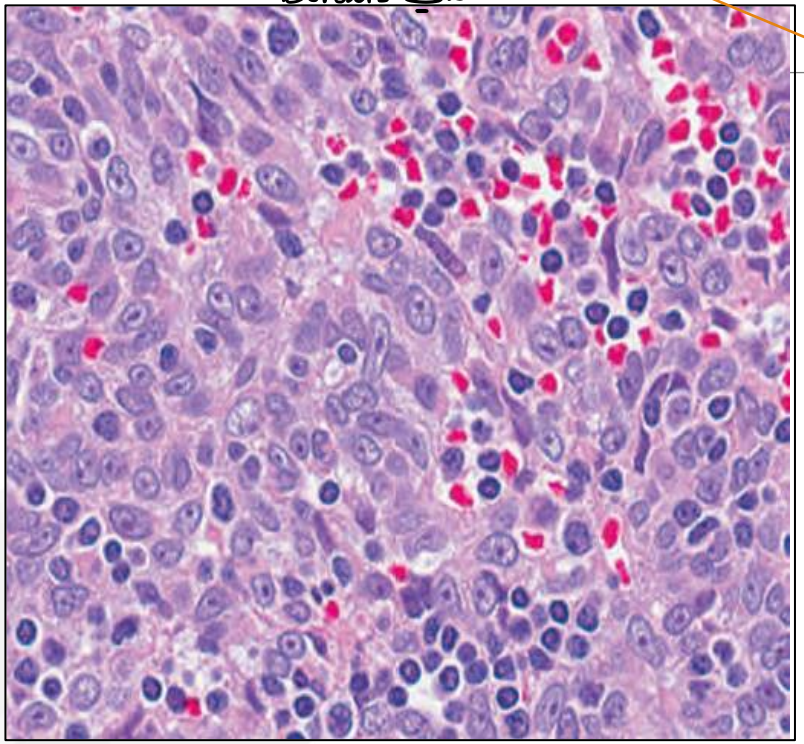
**Undifferentiated carcinoma**



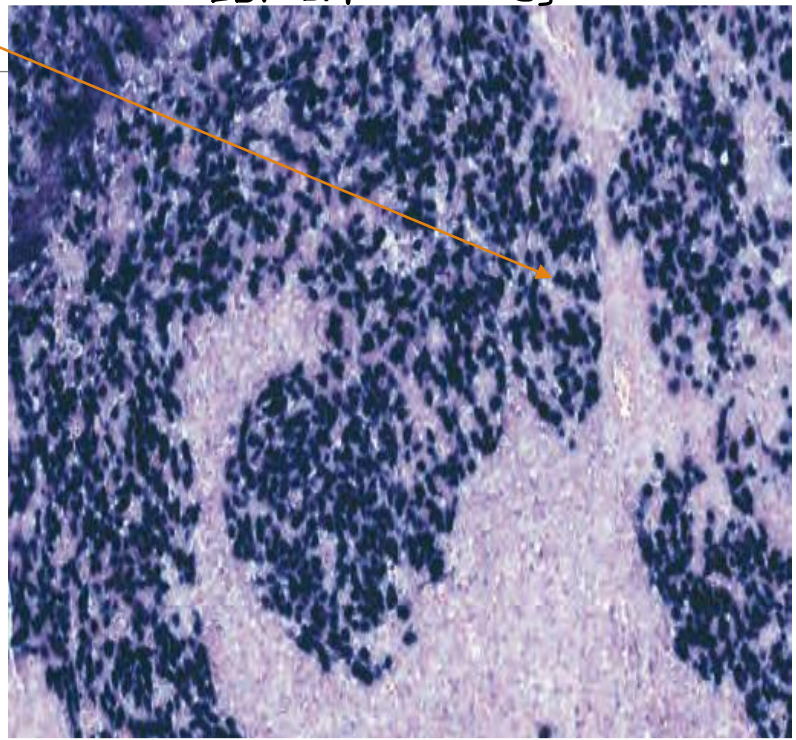

Small +dark

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

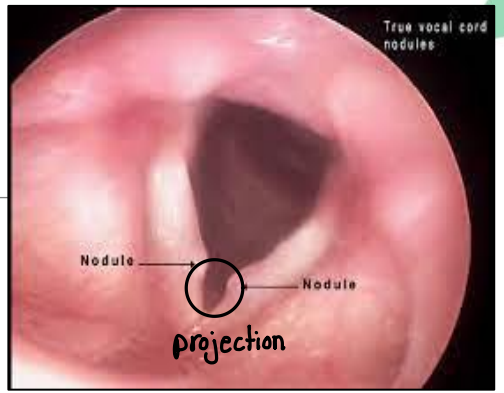
Borders حافي



هاد اللون :. positive لـ 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)

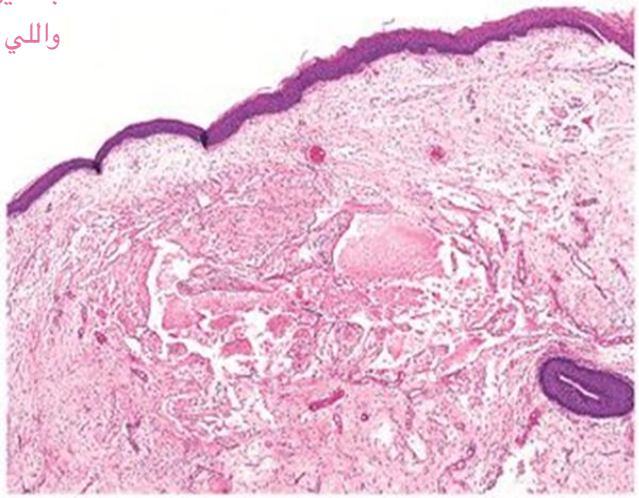
بتصير بالناس اللي ممكن يصير عندهم irritation بال vocal cords من ورا التدخين او كتر الاستخدام، زي المغنيين واللي بحكو كتير ⬅️ vocal cords nodules

**Histologically:** rounded

- Covered by squamous epithelium Benign
- The core of the nodule is a loose myxoid connective tissue that may be variably fibrotic or have numerous vascular channels.

ممكن fibrous tissue او blood vessels

- **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.**

Tips للـ finger


Histologically:

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

# Carcinoma Of The Larynx:

الأهم

- Mostly in 6th decade. بالكبار

- M>F (7: 1).

- Present as persistent hoarseness (بحة بالصوت), dysphagia (صعوبة بالبلع), and dysphonia (خلل بالحكي).

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

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

- The tumor develops directly on:
  - The vocal cords (**glottic tumors) most common** (80% *), or
  - Above the cords (supraglottic) or
  - Below the cords (subglottic).

مو شرط انو احنا نشخص الكانسر مباشرة وهو invasive
ممكن احيانا نقدر نشخصه بالمراحل الاولى والمريض بس عنده dysplasia ووقتها احتمالية انو يصير عنده invasive carcinoma
بتعتمد ع درجة dysplasia،، كل ما كانت severe اكتر كل ما كان المريض interest انو يصير عنده dysplasia اكتر ..

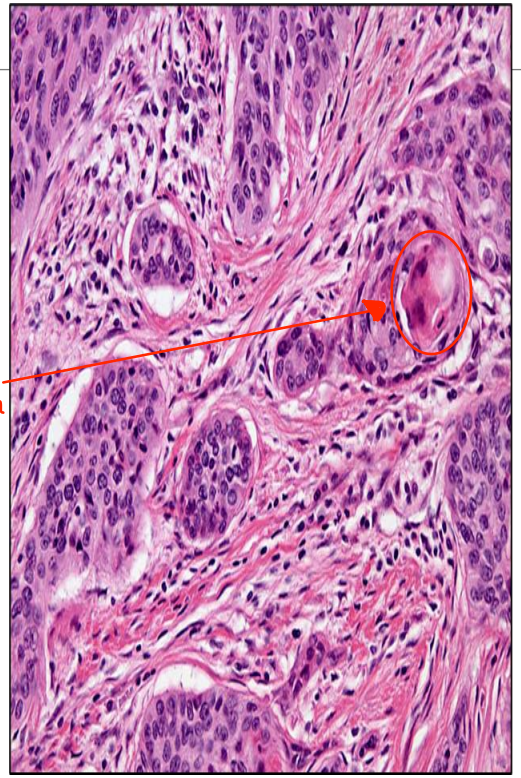
-**Grossly:** vary from white or reddened thickenings to irregular verrucous or ulcerated lesions.

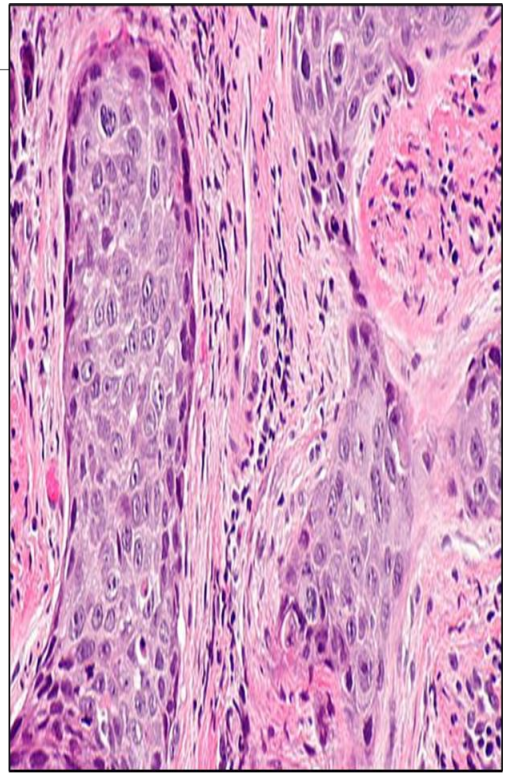
- The likelihood of the development of carcinoma is directly proportional to the grade of dysplasia when the lesion is first seen.

**Histologically:**

- About 95% are typical **squamous cell carcinomas.** Intercellular bridges,keratin formation

- Rarely, adenocarcinomas are seen.



very important *

## Prognosis (depends on the location):

ما بتنتشر وبتضل موجود ب larynx لانها بمنطقة true vocal cord ف بالتالي بتأثر ع true vocal cord ف بيجي المريض بأعراض مرحلة مبكرة وبنكتشفه وهو لساته confined لل larynx

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

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

- The **subglottic** tumors tend to remain **clinically quiescent** and usually present as **advanced disease.** بنكتشفهم بمراحل متأخرة (تحت vocal cord)

clinical manifestations ما بيعطو

Silent clinically

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

# Lower Respiratory Tract Pathology

Bronchi

Bronchiole بتتفرع ل

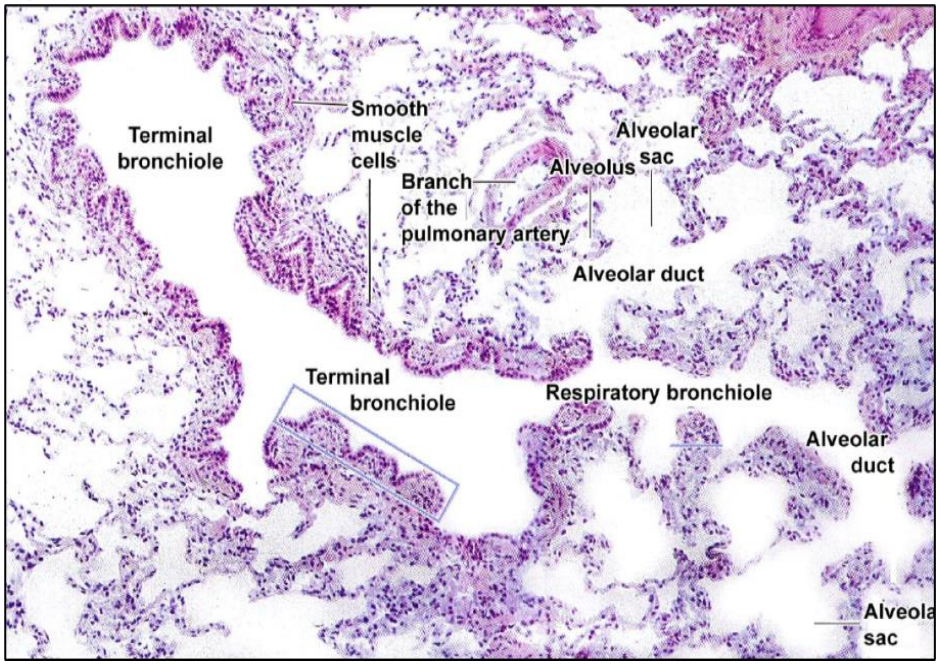
terminal bronchiole بنسميه bronchiole وآخر

acinus اسمه structure اللي بعده وال

مهم نتذكر الاناتومي والهستولوجي للـ lung

- 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:

Air sac: تبادل غازات

1. **The capillary endothelium and basement membrane.**

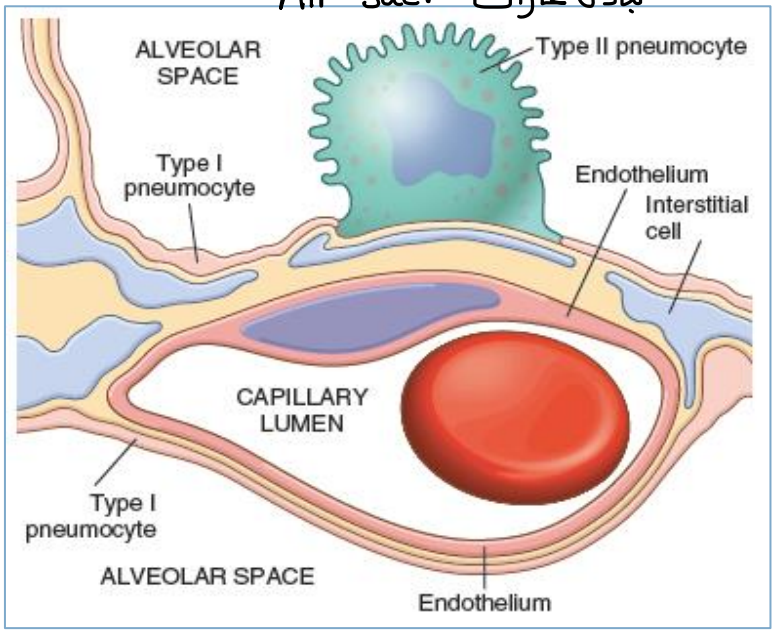
2. **The pulmonary interstitium** very thin: inflamatory cell

3. **Alveolar epithelium**

   - A flattened plate-like Type I pneumocytes (Flat cell). 95%

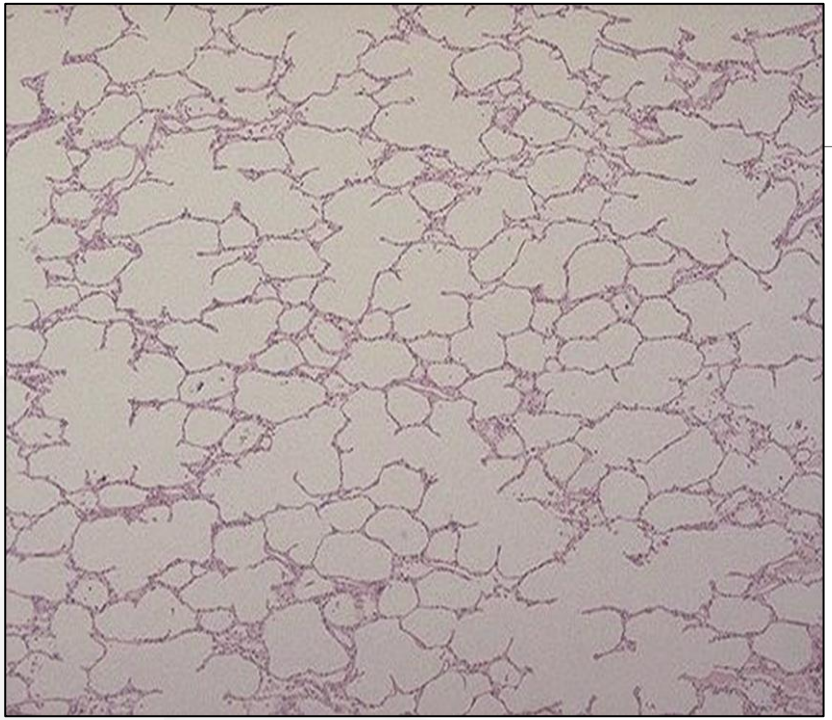
   - Rounded Type II pneumocytes (Rounded) (source of pulmonary surfactant (1) and involved in the repair (2) of pulmonary epithelium).

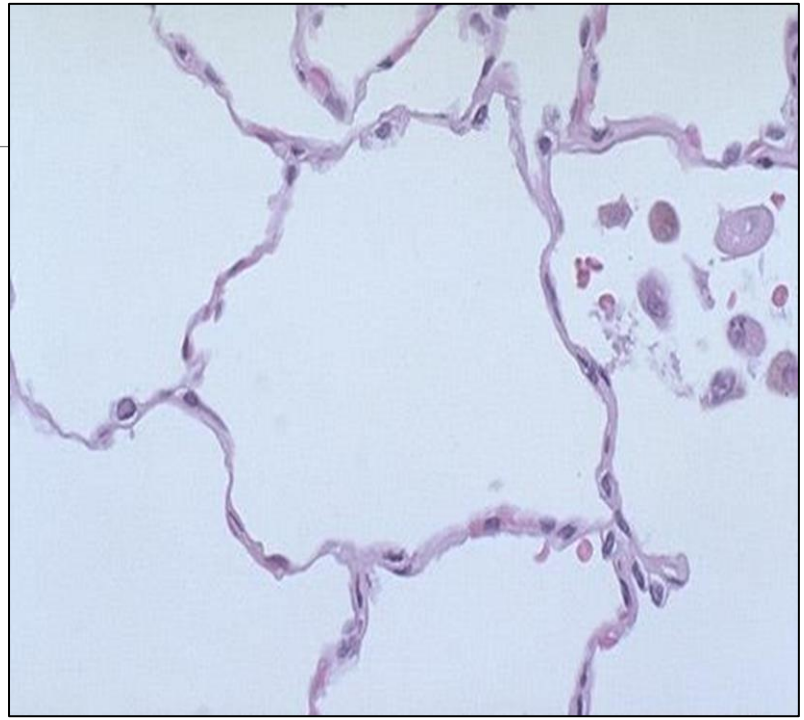
فاتحة alveolus بتخلي



# Normal histology للـ

#خلوها ببالكم





Very thin wall, Lined by pneumocytes, وجواها في alveolar macrophages

💡ال Atelectasis و ARDS همه general patterns يعني ممكن يصيرو مع كتير امراض ..

# Atelectasis (COLLAPSE)

تسكير بـ lung

- **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.**

ال alveoli سكرت ف مافي تبادل غازات

Outcomes depend on:

1- Cause.

2- Size of involved area.

3- Duration to start treatment. سرعة العلاج

irreversible *

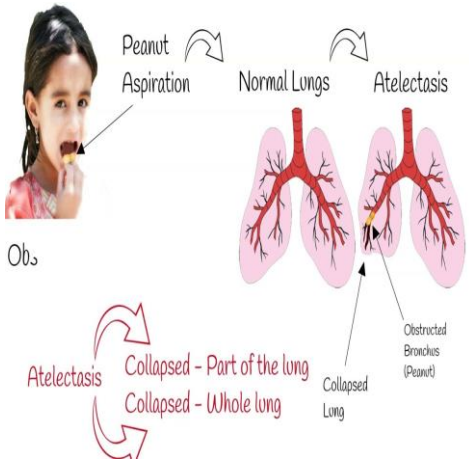
Atelectasis (except when caused by contraction) is potentially **reversible**

# Types of Atelectasis : حسب السبب

## I- Resorption atelectasis :

في شي سكر air way زي mucus وهاد ادى ل alveoli امتصاص الهواء وبعدين سكرت

- Occurs when **obstruction** (السبب) prevents air from reaching distal airways.
- The air already present becomes absorbed & alveolar collapse follows.
- An entire lung (رح تصغر), 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 (عند الاطفال خصوصًا) and tumors.




**Mediastinal Shift to Same Side**

لأنو Lung صغرت وصار في مساحة

## II- Compression atelectasis :

تسكير بسبب ضغط ، يعني في شي عم يضغط عالرئة من برا ويعمل تسكير لأكياس الهوا مثل fluid او هواء

- 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.

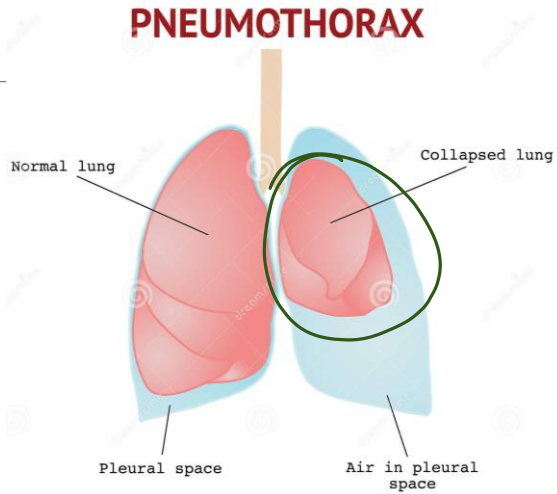
- This frequently occurs with **pleural effusion** and **pneumothorax.**

Fluid

air

- Maybe caused by an elevated diaphragm.

* سبب آخر




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.** **

Collapse ← lung بتأثر ع حركة

## IV- Microatelectasis:

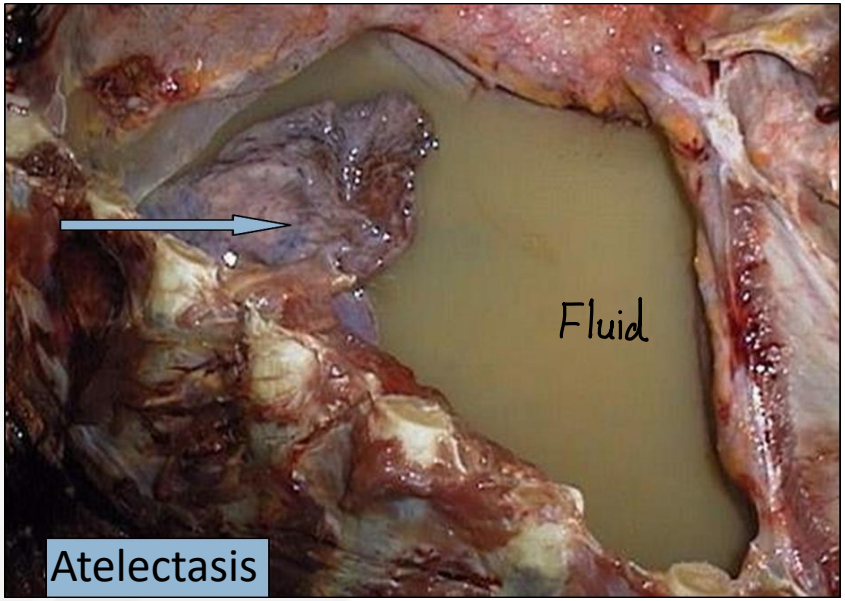
بمنطقة صغيرة

- Due to loss of surfactant.

# Morphology of Atelectasis :

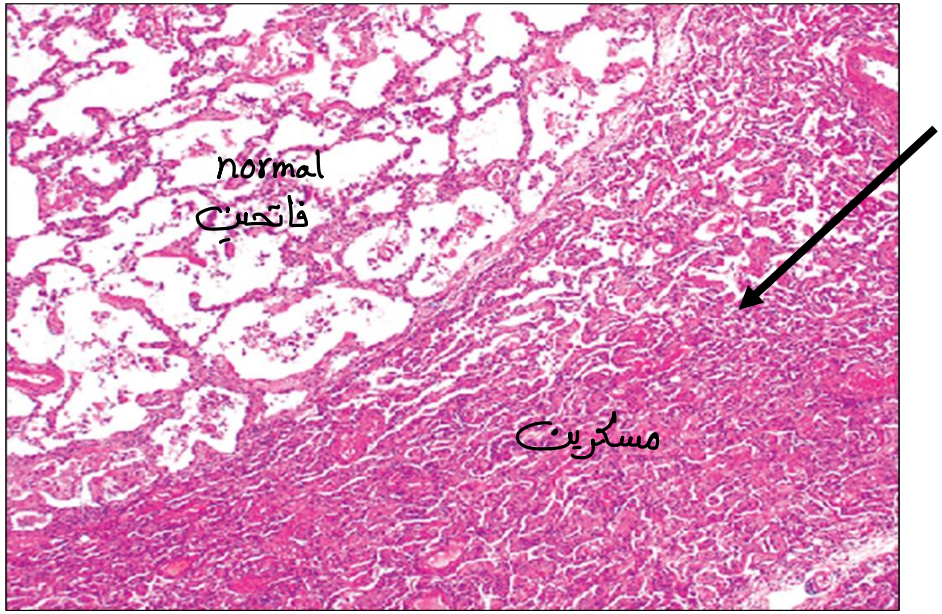
## Gross:

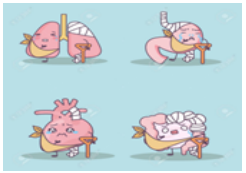
- Shrunken lung.




## Microscopic:

-Slit-like alveoli, congested septae.





# Acute Respiratory distress syndrome (ARDS):

clinically ↑

- A severe form of acute lung injury.

- Clinical syndrome that is caused by many conditions. مو مجرد مرض واحد

- Characterized clinically by:

  - Sudden and Acute onset of severe dyspnea. *

  - Severe arterial hypoxemia, hypercapnia ($\uparrow CO_2$) and cyanosis

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

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

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

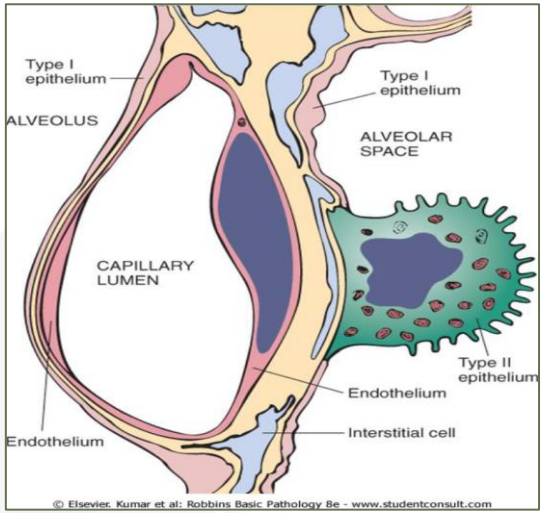
- **The above-mentioned manifestations should happen in the absence of left-sided heart failure.** * → شرط حتى احكي انه ARDS

# Etiology:

**Sepsis & pneumonia account for 40-50% of cases**

| Direct lung injury | Indirect lung injury |
|---|---|
| # المطلوب **Common causes** | |
| ***Pneumonias*** infection in lung | ***Sepsis*** |
| ***Aspiration of gastric content*** شرق ← محتويات المعدة طلعت لـ lung | ***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:




Injury → يتأثر

-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. ⇒ Collapse

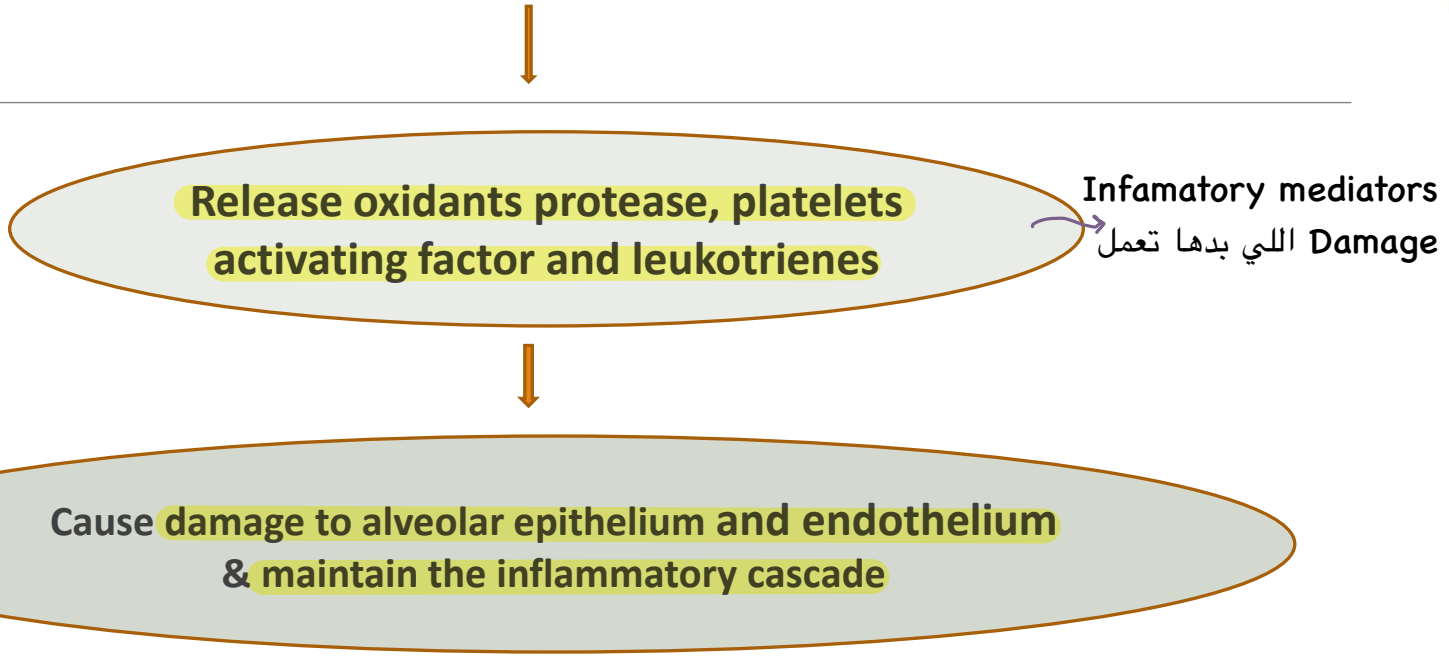
Early after **injury** ➡ increased synthesis of

**IL 8** by pulmonary **macrophages**.

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

neutrophil يجذب

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



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

مقاومة :-

- 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.

distrustion الأقوى هو اللي رح يحدد كم حيكون في عنا

## ***Later:***

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

Healing

بمراحل متقدمة

# Morphology (phases of ARDS):

## - Acute/Exudative phase:

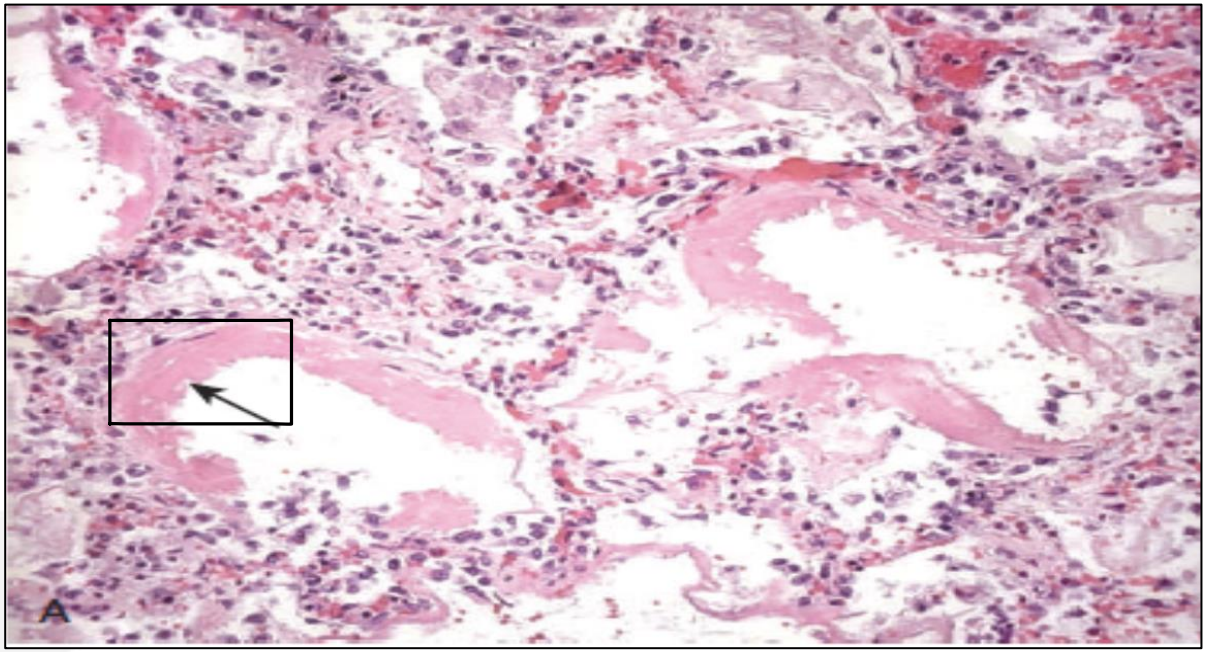
- The lungs are red, firm, airless, and heavy. (distruction)

**Microscopically:**

- There is capillary congestion.
- Interstitial and intraalveolar edema & hemorrhage, and collection of neutrophils in capillaries. (infection لوفي)
- Necrosis of alveolar epithelial cells
- Collapse of alveolar parenchyma
- The most characteristic finding is the presence of hyaline membrane lining the distended alveolar ducts.

تجمع لبقايا الخلايا اللي ماتت مع fibrin والبروتين
اللي بطلع من الدم ، necrotic Cells

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



**Organizing/ proliferative phase:** Healing

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

يصير proliferation لل fibroblasts ع أساس انها تعمل
organizing وتحاول تلم منطقة injury ويتحول hyaline

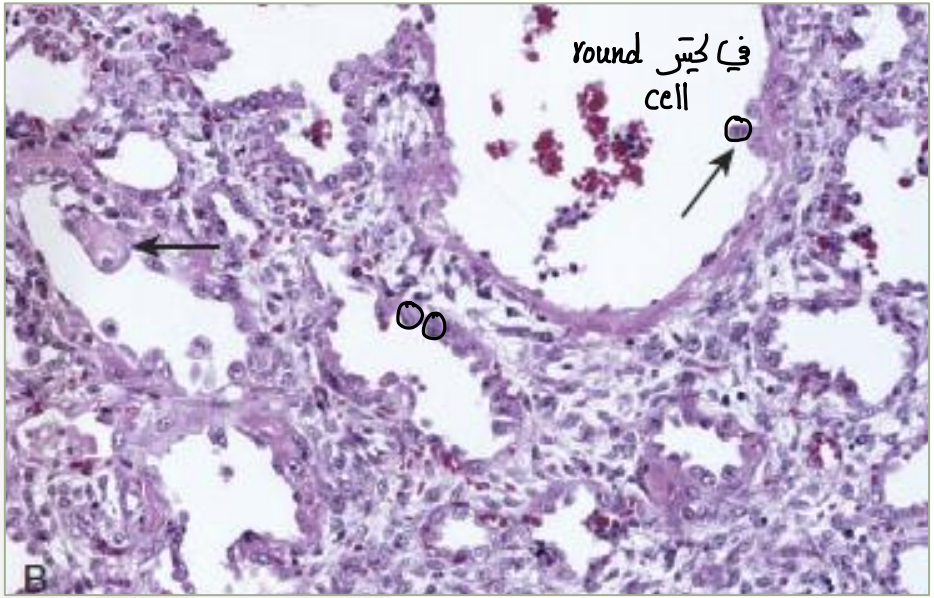
- Resolution is unusual; more commonly, there is an organization of the fibrin exudates with resulting **intra-alveolar fibrosis (organizing pneumonia (OP)).** alveoli جوا ال fibrosis ل membrane

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

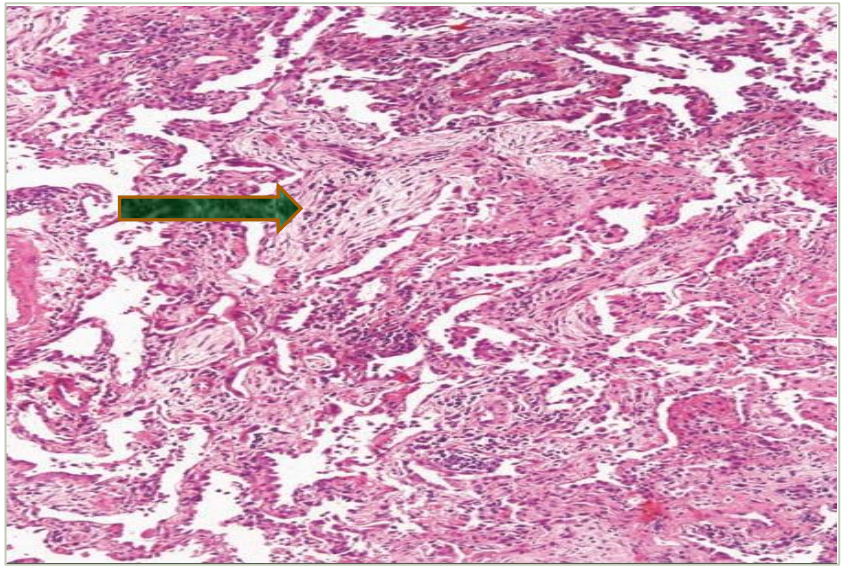
**Fibrotic phase:** **Usually, after several weeks on a respirator.** end stage # not important

proliferation of reactive **type II pneumocytes**

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):** intra-alveolar fibrosis



# Clinical course : Mortality ↑↑ حسب عوامل

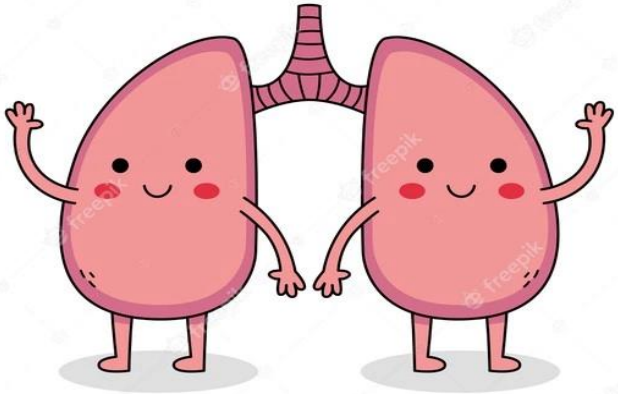
- **85%** of patients develop the clinical symptoms within 72 hours of the initiating insult.

**-The predicting factors in ARDS are:**

في ناس بعدو مرحلة acute injury وبرجعو طبيعين ، وفي نسبة كبيرة بضل عندهم clinical manifestations و defect ب respiration لمرحلة طويلة وفي ناس ممكن يموتوا

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

poor outcome



بالتوفيق ..🤍

Thank You

dana