# Pathology of the Respiratory System-3

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## *-Emphysema*

**Definition:**

Permanent enlargement of the air spaces distal to the terminal bronchioles (resp. bronchiole ,alveolar duct and alveolus) with destruction of their wall without apparent fibrosis.

**Incidence:**

- Common in minor degrees(~50% of autopsy) but missed.
- May coexist with chronic bronchitis (COPD).

**Clinical course** -

Progressive dyspnea ± cough ↓ FEV1 ,Barrel chest , Pink Puffer, but when there are elements of chronic bronchitis and repeated chest infection these may lead to hypercapnia, chronic Hypoxia, cyanosis (blue bloater) , Pulmonary Hypertension and cor pulmonale.

## Pathogenesis :

**(Protease/ Antiprotease imbalance)**

- Excess protease or elastase activity is unopposed by appropriate antiprotease ( $\alpha$1AT).

- Decrease in antiprotease activity may be :

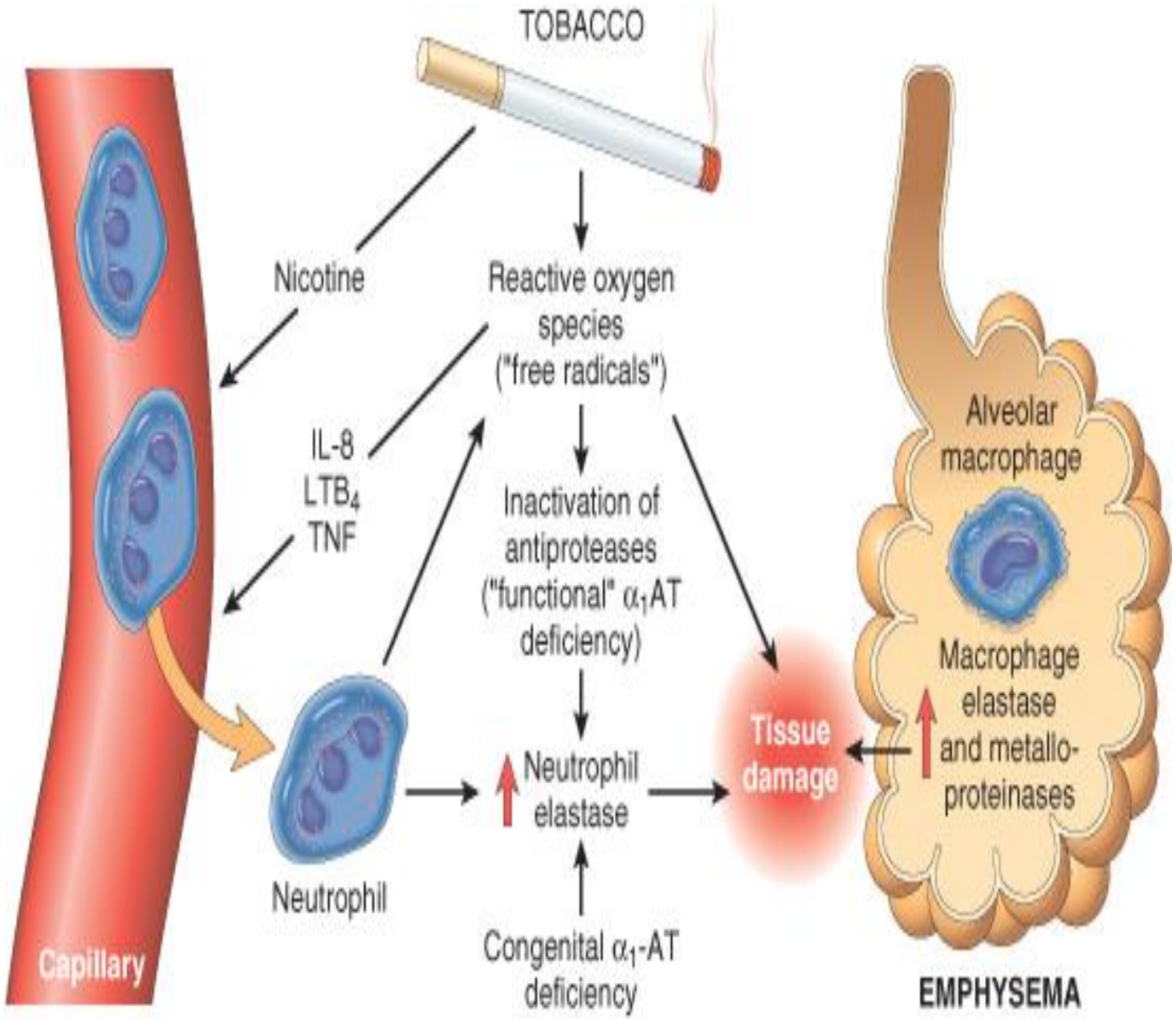
i- Genetic: $\alpha$1 antitrypsin deficiency (mutant $\alpha$1AT accumulates

in ER of hepatocytes which results in liver damage.) .

ii- Acquired: Smoking inhibits enzyme activity, and increase protease occurs whenever there is increase in neutrophils & macrophages.

- **Result** :

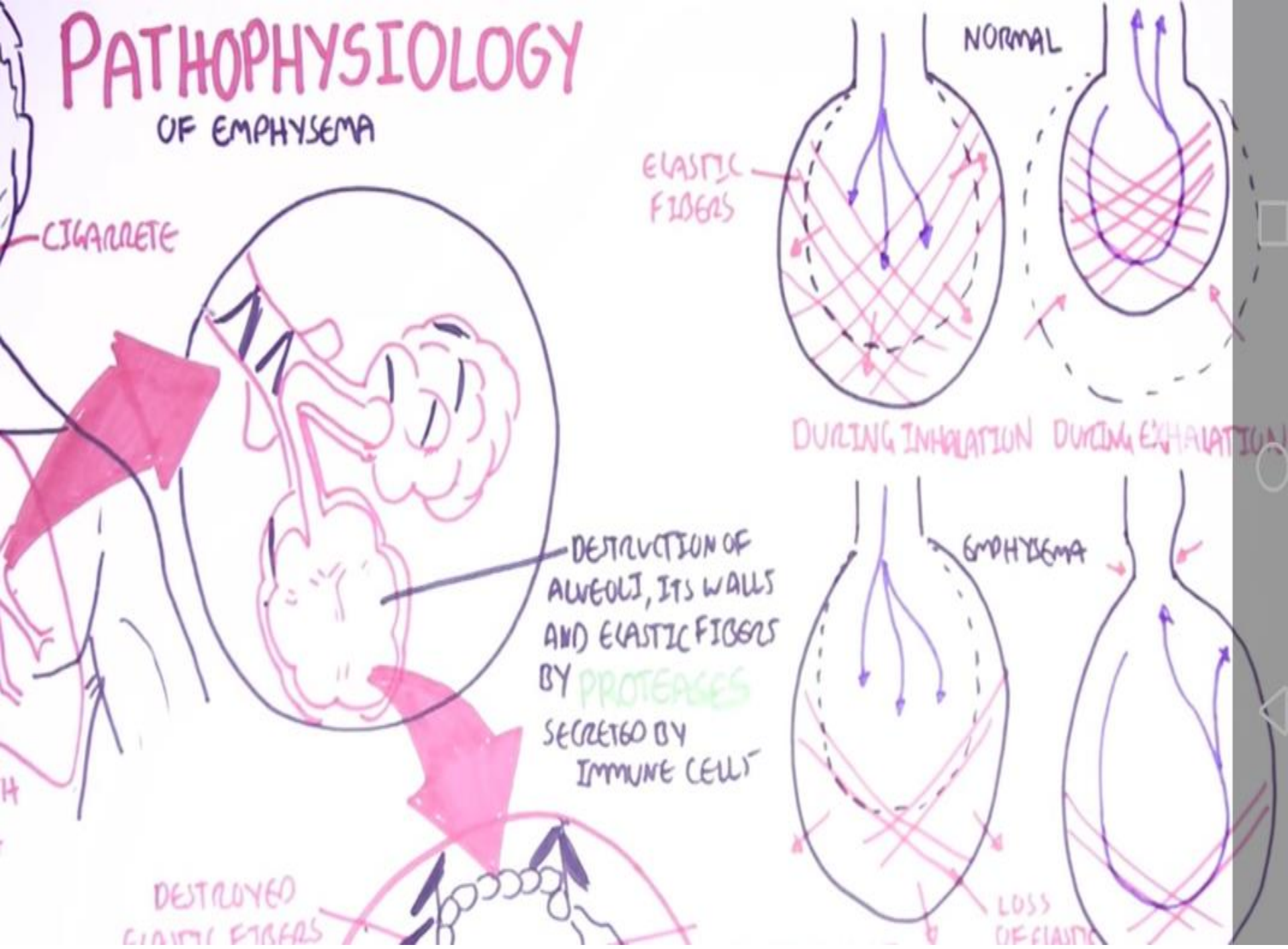
Elastic tissue digestion & destruction $\rightarrow$ EMPHYSEMA




# Pathogenesis of emphysema

# PATHOPHYSIOLOGY

## OF EMPHYSEMA



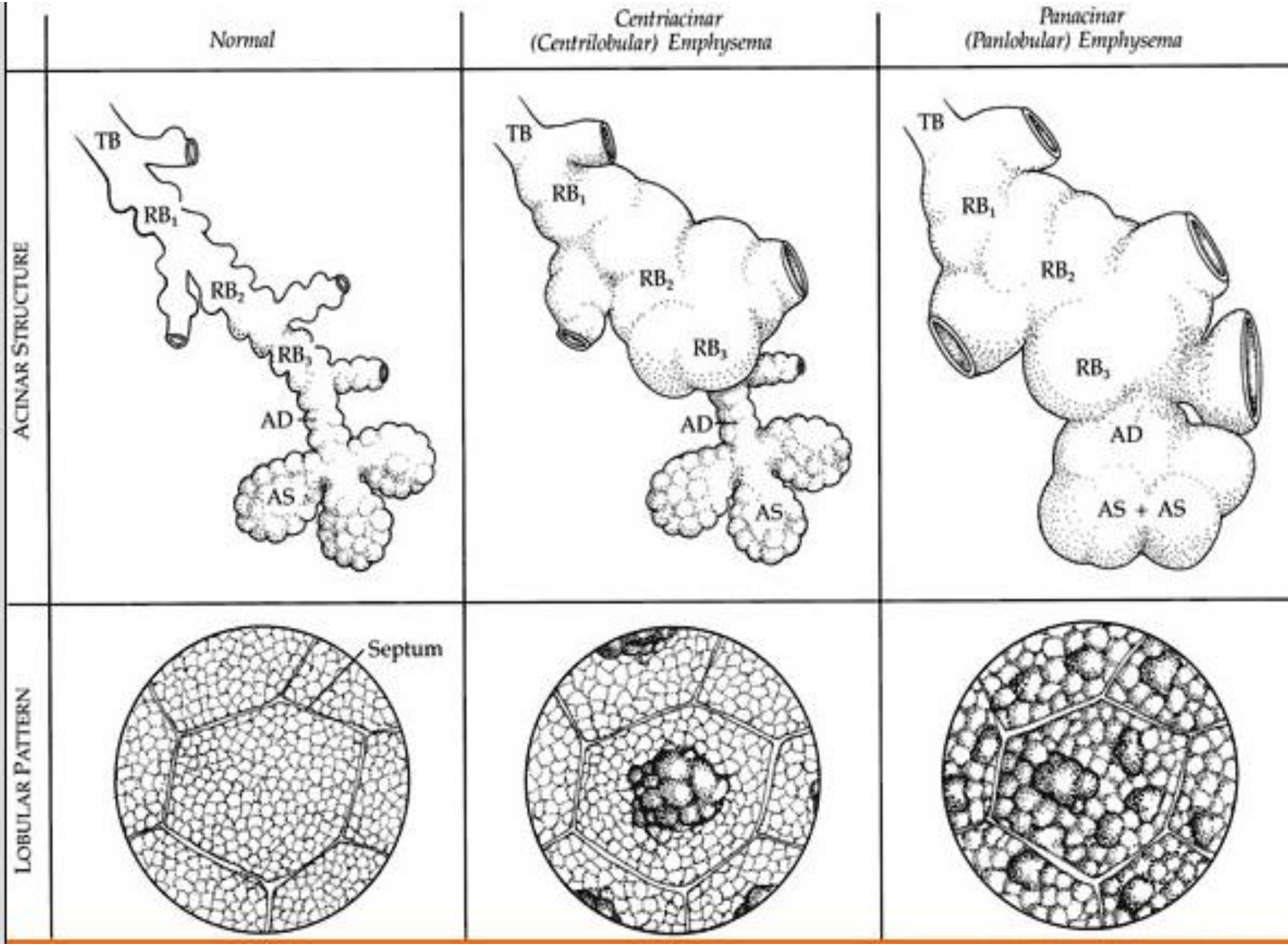
# Types of emphysema:

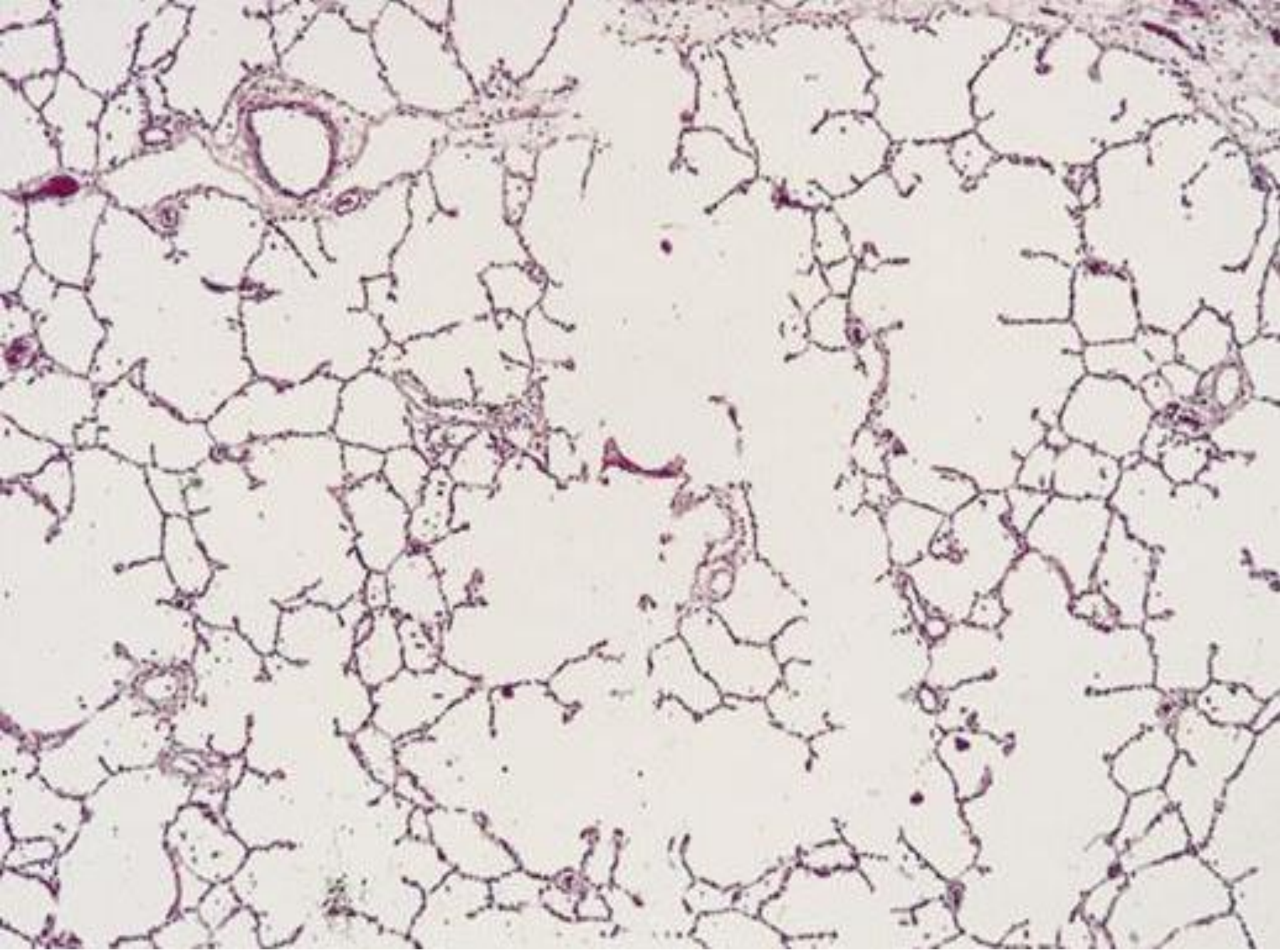
## *I- Centriacinar (centrilobular) emphysema:*

- Involves the proximal part of the acinus ( respiratory bronchiole ) i.e. center of the lobule
- More severe in upper lobes
- ~ Inflammation around bronchi & bronchioles
- More in male, smokers and in ass. with chr. bronchitis.
- In severe cases: difficult to differentiate from panacinar type.

## *II- Panacinar (Panlobular) emphysema:*

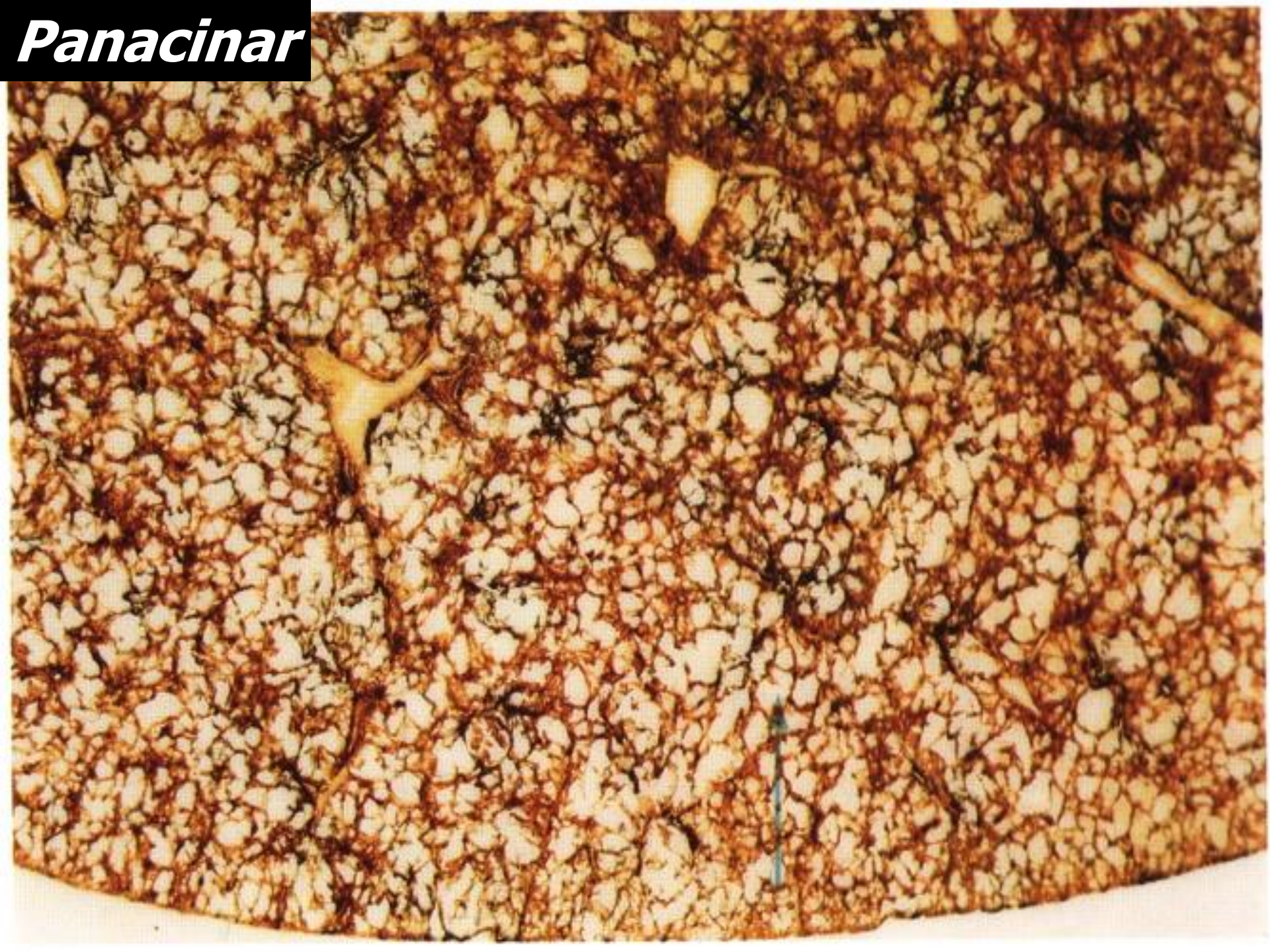
- Involves entire acinus from respiratory bronchiole down to blind alveoli.
- More severe in lower zones & bases
- High association with $\alpha$1 antitrypsin deficiency.


Normal
Centriacinar (Centrilobular) Emphysema
Panacinar (Panlobular) Emphysema
ACINAR STRUCTURE
LOBULAR PATTERN
TB
RB1
RB2
RB3
AD
AS
AS + AS
Septum




Centriacinar

# Panacinar



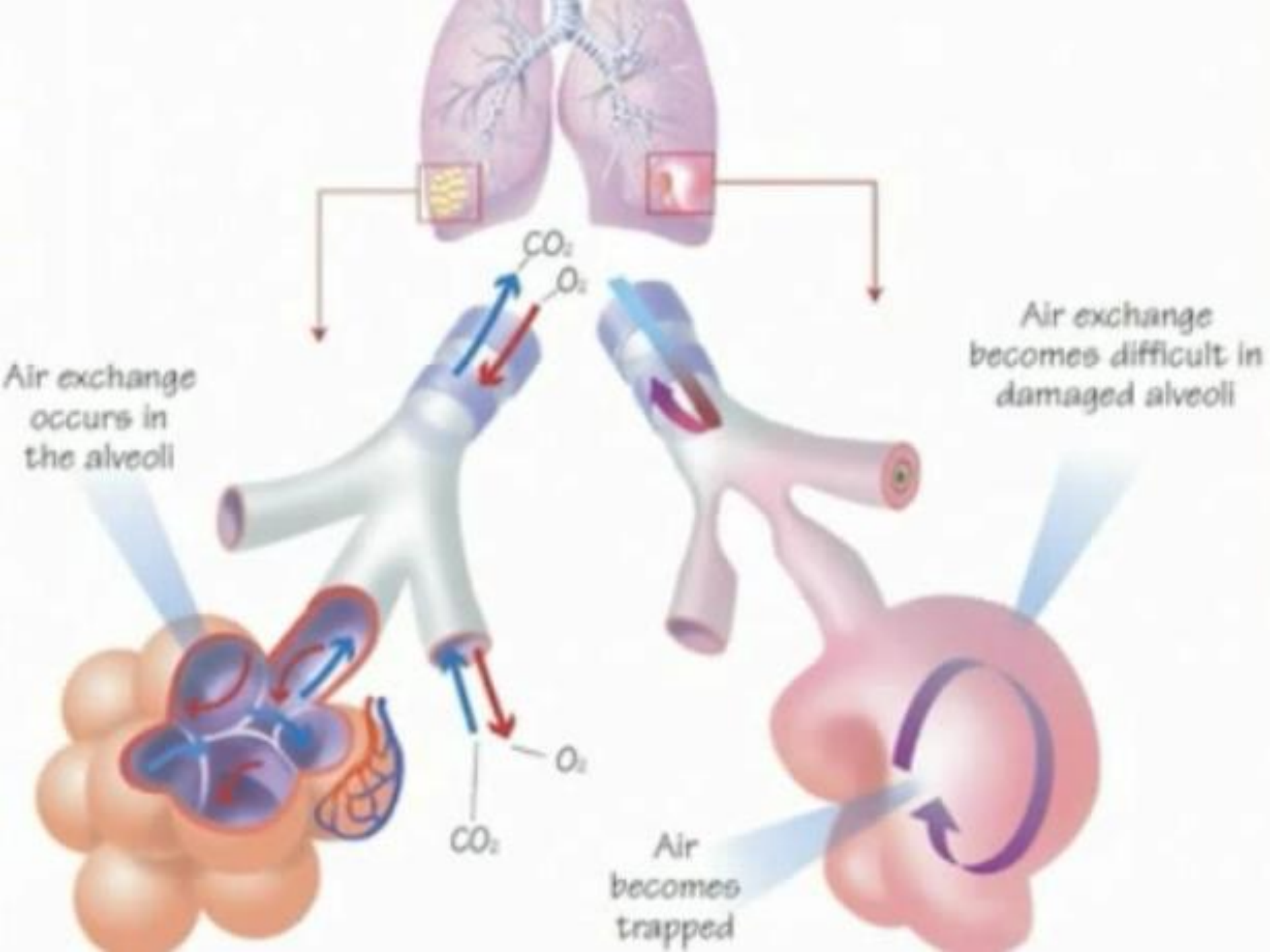
## Morphology

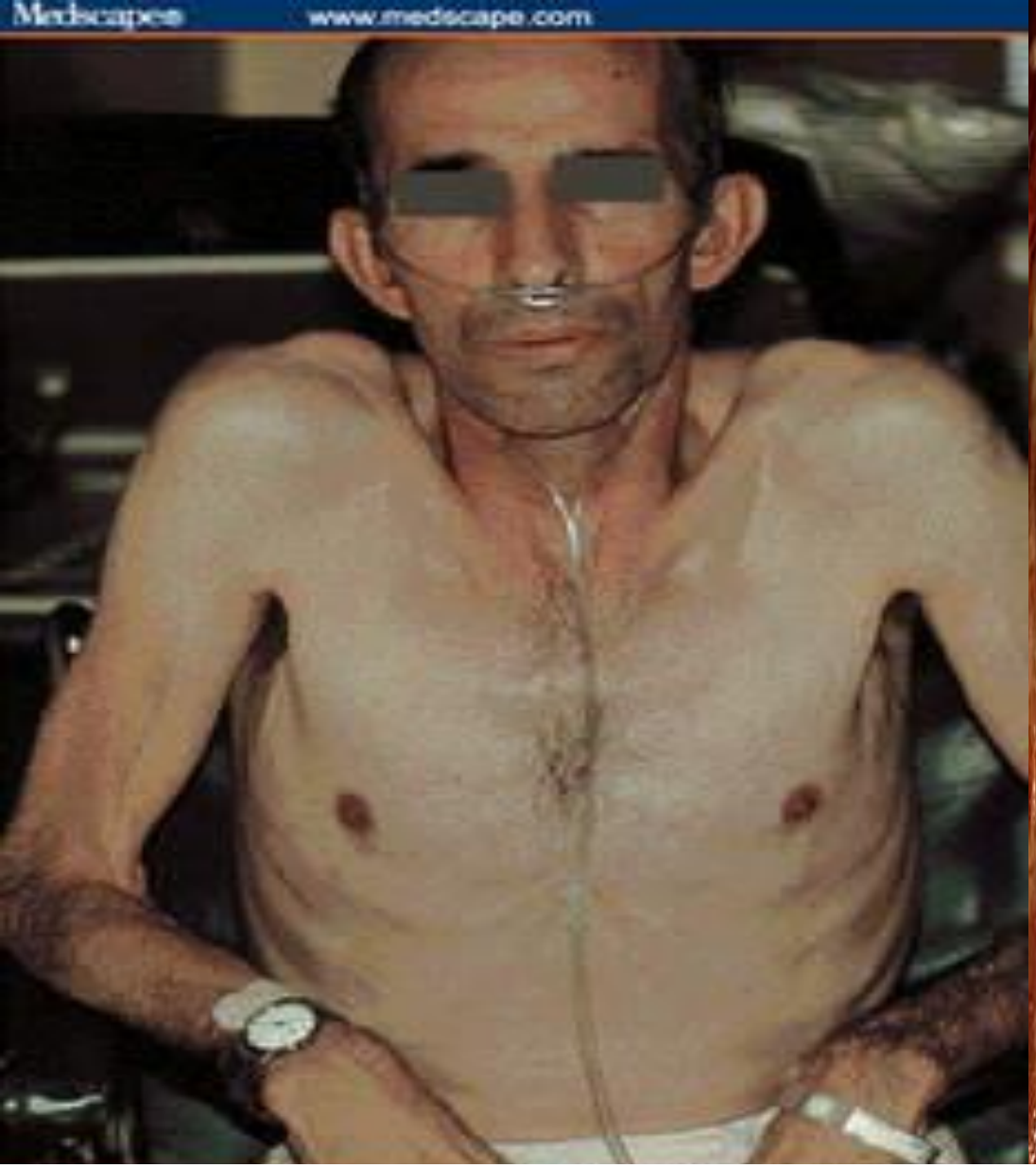
Macroscopic:

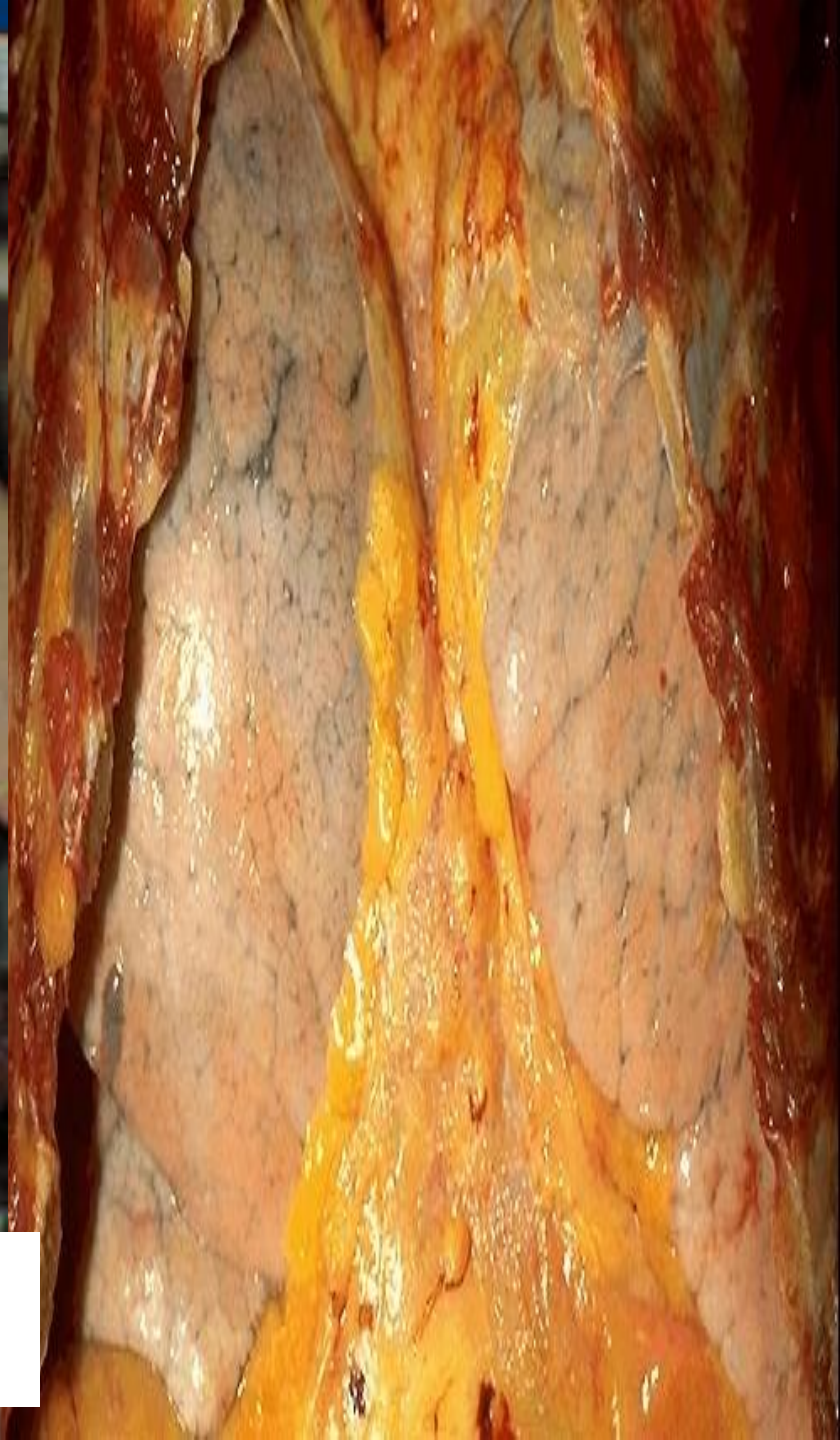
- Large pale lungs ,may obscure the heart, less severe in centriacinar where it is more in upper lobes.

Microscopic :

- Destruction of alveolar walls $\rightarrow$Confluent air spaces with loss of elastic tissue … not effectively expelling air.
- Normally, elasticity of air sacs attached to bronchioles keeps the bronchiole open during expiration, here the bronchioles will collapse during expiration.
- Collapse of adjacent spaces ,diminished vessels in septae, chronic bronchitis may be seen.
- Later pulmonary hypertension & cor pulmonale.


Air exchange occurs in the alveoli
Air exchange becomes difficult in damaged alveoli
$CO_2$
$O_2$
$O_2$
$CO_2$
Air becomes trapped



- **Emphysema patient (so-called pink puffers) exhibit dyspnea without significant hypoxemia and tend to be thin ( use muscle for breathing)**

## *III- Distal (Paraseptal) emphysema:*

- Mainly along pleura & connective tissue of septae
- More in upper lobe.
- Adjacent to fibrotic areas of previous inflammation or atelectasis.

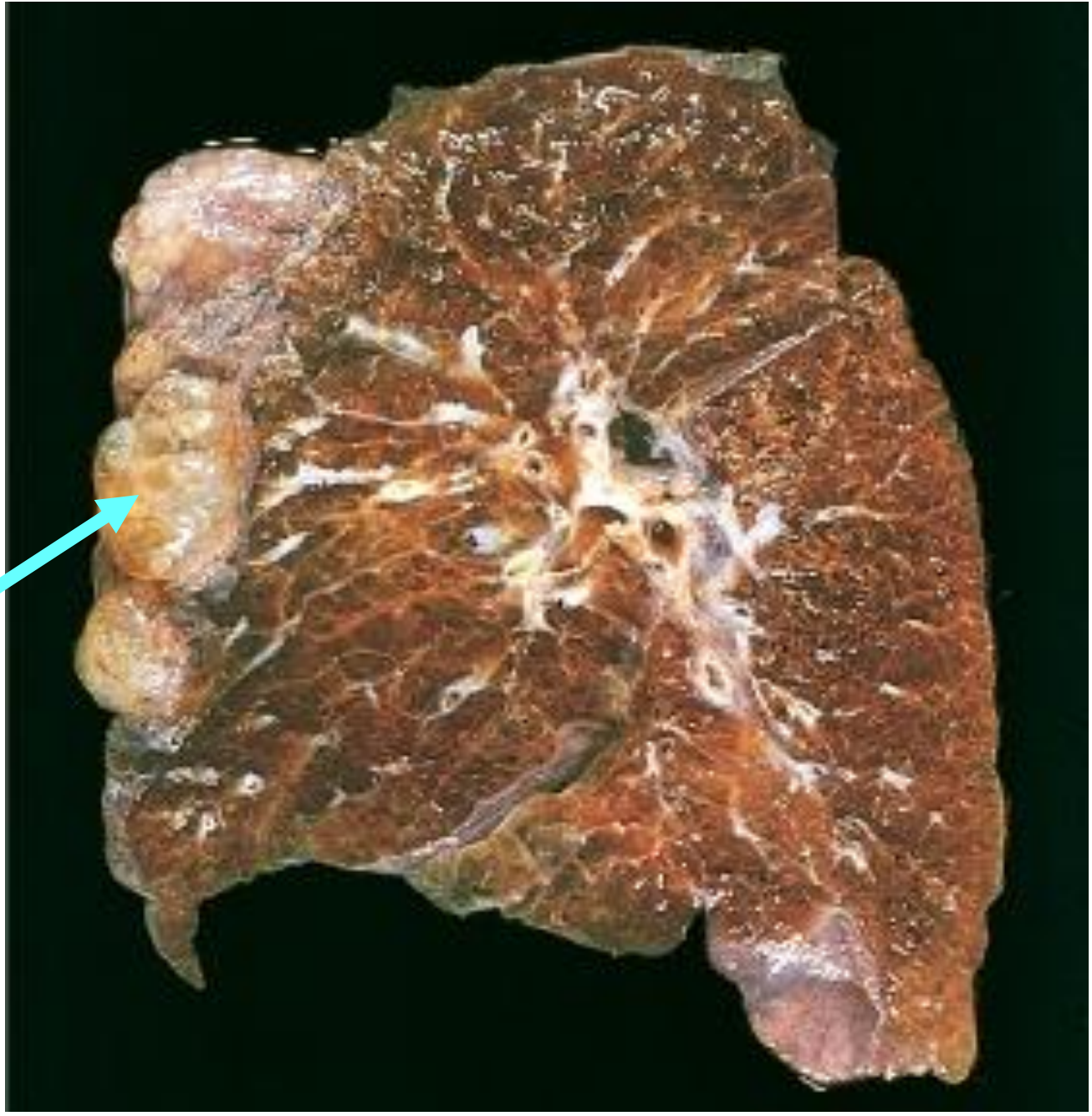
**Bullous Emphysema:

-Formation of sub- pleural air filled cysts (0.5-2cm.or more) in any type, but more in paraseptal.

-May lead to *Pneumothorax.*

***interstitial emphysema:*

Refers to entrance of air to lung stroma , mediastinum or subcutaneous tissue (by alveolar tear or #ribs)



**Bullous Emphysema**

# Pathology of the Respiratory System-4

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## Chronic Bronchitis

- Persistent cough with sputum production for at least 3 consecutive months for at least 2 consecutive years.

**Imp. definitions:**

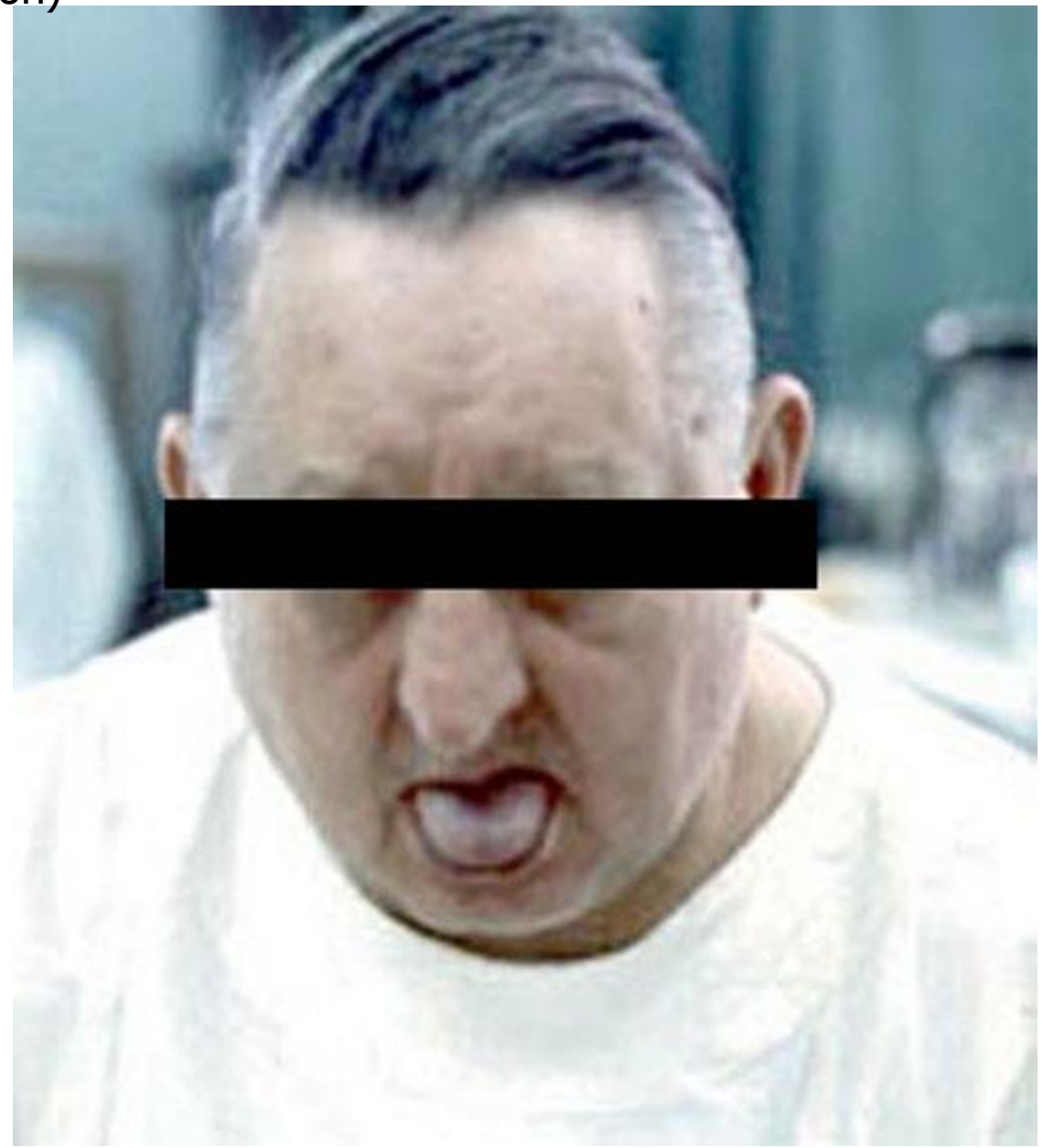
1- Simple chronic bronchitis→ mucoid sputum(no obstructive symptoms).

2- Chronic mucopurulent bronchitis (infection).

3- Intermittent bronchitis with hyperactive airway and bronchospasm= chronic asthmatic bronchitis.

4- Obstructive chronic bronchitis when there is obstructive symptoms, usually associated with emphysematous changes.

**Chronic productive cough with large amount of sputum, accompanied by hypercapnia, hypoxia ± cyanosis (blue bloater) → Cor pulmonale(**low O2 induces vasoconstriction)



## Pathogenesis :

Ch. Bronchitis represents reaction of the tracheobronchial tree to inhaled irritants e.g. Cigarette smoke, this induces Hypersecretion of mucus by :

1-Hyperplasia & hypertrophy of mucus glands

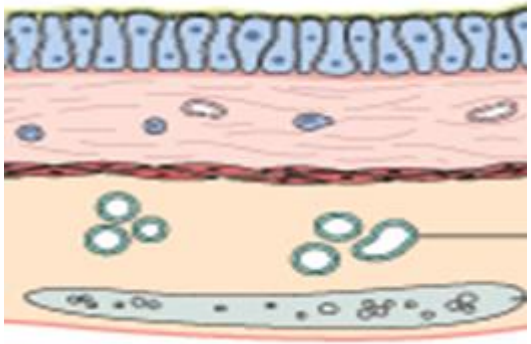
2-Increase in goblet cells by metaplasia

3-Recurrent infections(~ it does not initiate the condition but exacerbates the dz).

***Macroscopy:*** Edematous congested bronchus with luminal thick mucus.

***Microscopically :***

Inflammatory cell infiltrate, enlarged mucus gland layer, ↑number of glands,~↑ goblet cells down to small passages, metaplastic changes (of goblet & squamous cells ) ± Dysplasia.



**Reid Index** : Thickness of mucus layer / bronchial wall (normally ~0.4) but Increased in chronic Bronchitis.

## - Bronchiectasis

A permanent dilation of bronchi and bronchioles due to chronic necrotizing infection that causes destruction of the muscle & elastic tissue. Loss of muco-ciliary clearance system is the main problem.

Predisposing conditions include:

1-Congenital & hereditary conditions : -

- -Cystic fibrosis, Immunodeficiency, Kartagner's S *(Sinusitis, Infertility, Inversion of body organs, Bronchiectasis).*

2-Bronchial Obstruction:

- Localized (F.B. or Tumor)
- Generalized (asthma, bronchitis)

## Morphology :

-Localized or widespread, but more in lower lobes.

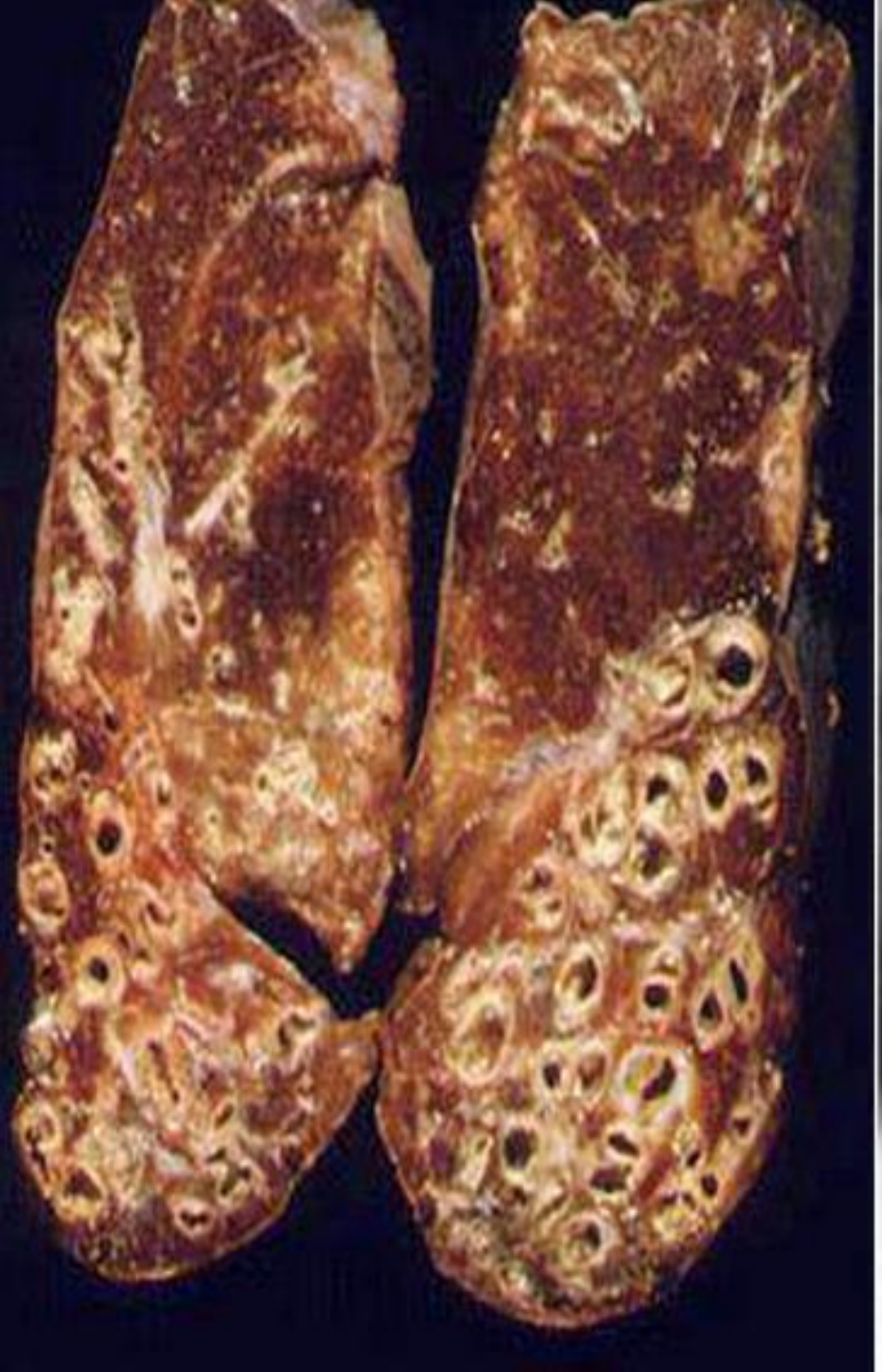
-Dilatation can be followed almost to pleural surface.

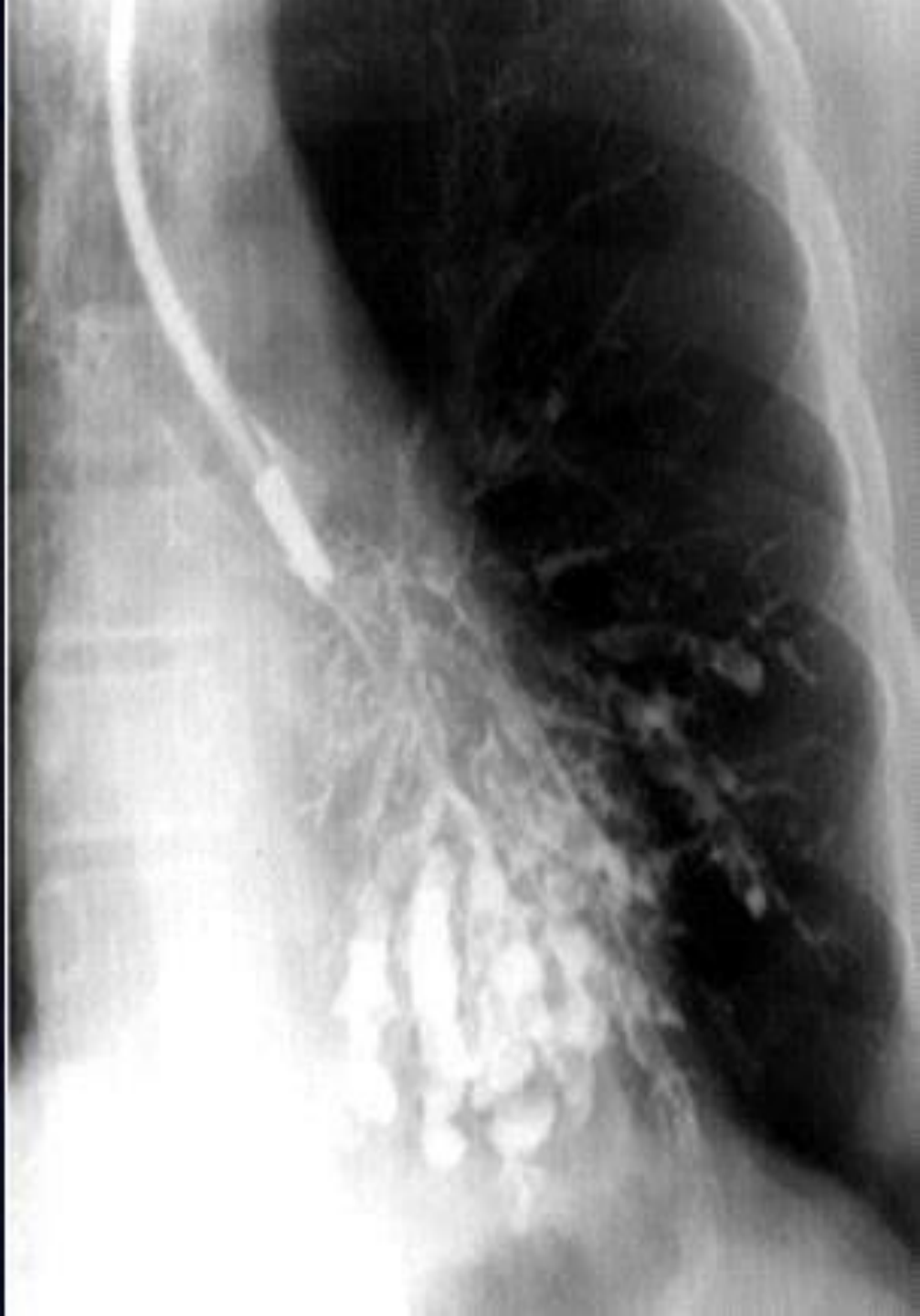
-Wall shows acute & chronic inflammatory cells with squamous metaplasia of lining +fibrosis.

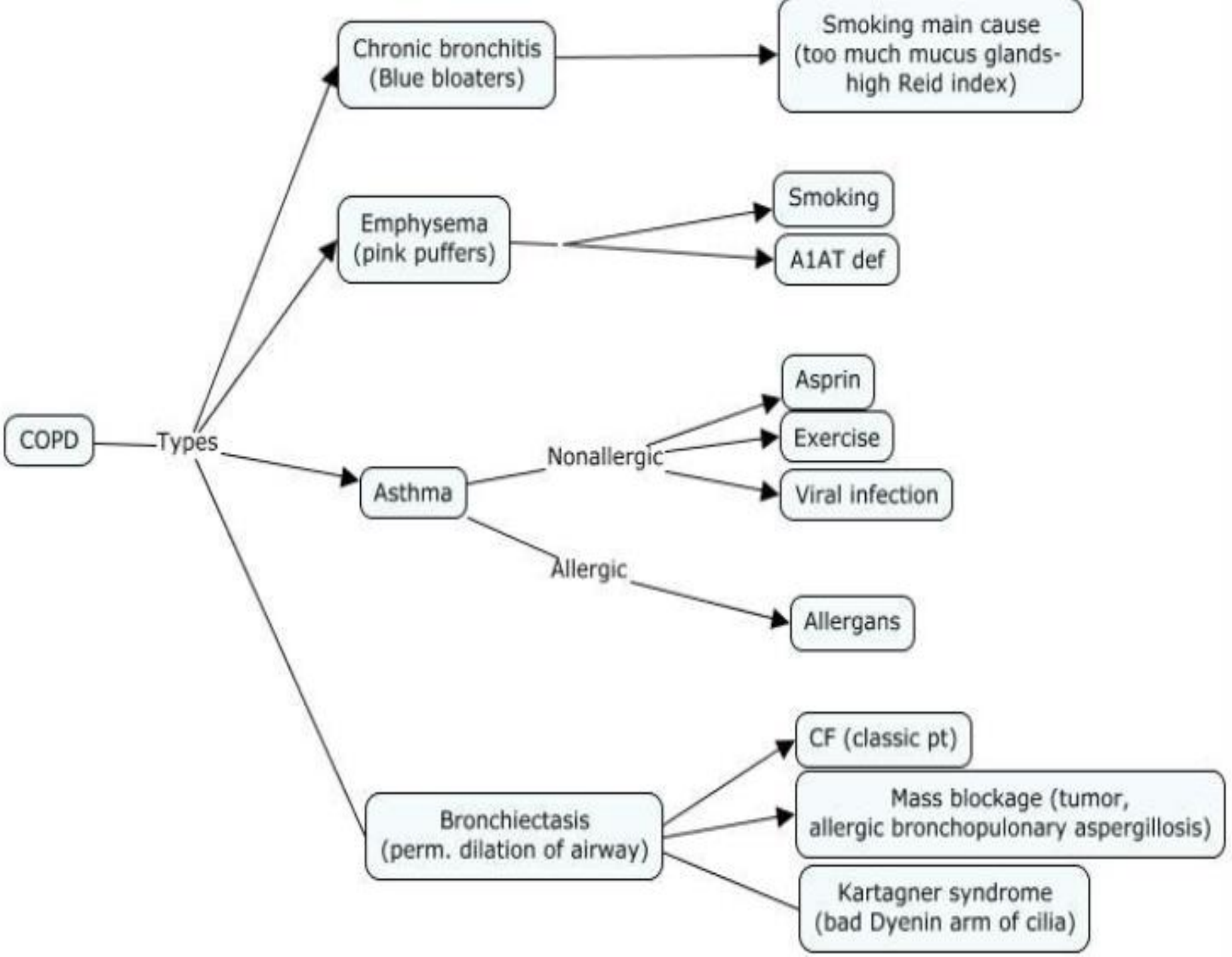
**Clinical:** Chronic productive cough with purulent sputum and hemoptysis.

## Complications of Bronchiectasis

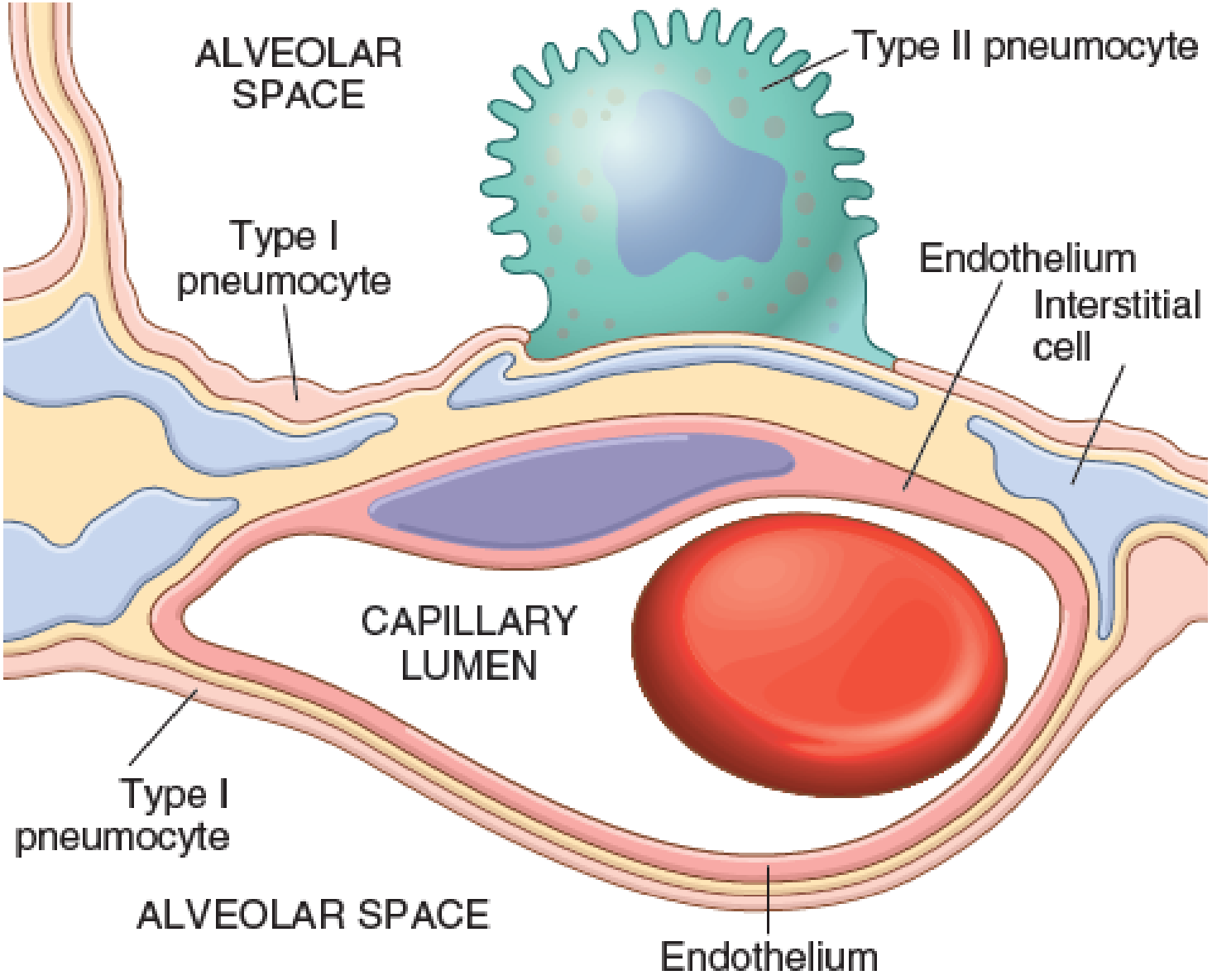
- Bronchopneumonia ,Lung Abscess , Metastatic abscess e.g. brain abscess , amyloidosis and obstructive Lung diseases $\rightarrow \uparrow$ Pulmonary Pressure and Cor pulmonale.






COPD
Types
Chronic bronchitis (Blue bloaters)
Smoking main cause (too much mucus glands- high Reid index)
Emphysema (pink puffers)
Smoking
A1AT def
Asthma
Nonallergic
Asprin
Exercise
Viral infection
Allergic
Allergans
Bronchiectasis (perm. dilation of airway)
CF (classic pt)
Mass blockage (tumor, allergic bronchopulonary aspergillosis)
Kartagner syndrome (bad Dyenin arm of cilia)

# RESTRICTIVE LUNG DISEASES




**Alveolar wall structure**

# ***Restrictive lung diseases:***

Characterized by reduced lung volumes, either because of an alteration in lung **parenchyma** or because of a disease of the pleura, chest wall, or neuromuscular apparatus and characterized by:

- ↓ Vital Capacity (Forced vital capacity -FVC )
- Forced expiratory Vol.( FEV1 ) is almost normal.

- In parenchymal type it can lead to progressive dyspnea, hypoxia (due to interference bet. alveolar space and blood by fibrosis), pulmonary hypertension, respiratory failure & cor pulmonale.

# *A-Acute Restrictive Lung Diseases*

## I-Acute Respiratory Distress Syndrome :

Defined as rapid respiratory failure with bilateral opacities on chest imaging, not fully explained by effusions, atelectasis, cardiac failure, or fluid overload.

- **Causes:**

-**Pneumonia** (≈45%), **sepsis** (≈ 35%), aspiration, trauma, surgery, multiple #, pancreatitis ……

**-Pathogenesis:**

? Activation of macrophages/neutrophils…releases protease & free R➢mage endothelial cells and pneumocytes (DAD)➢ oozing of proteins with surfactant deficiency ➢ Hyaline membrane formation.

In Chemicals agents>> direct alveolar damage>> DAD

## Pathology :

Lung appears dark , red , airless and heavy.

## Microscopically:

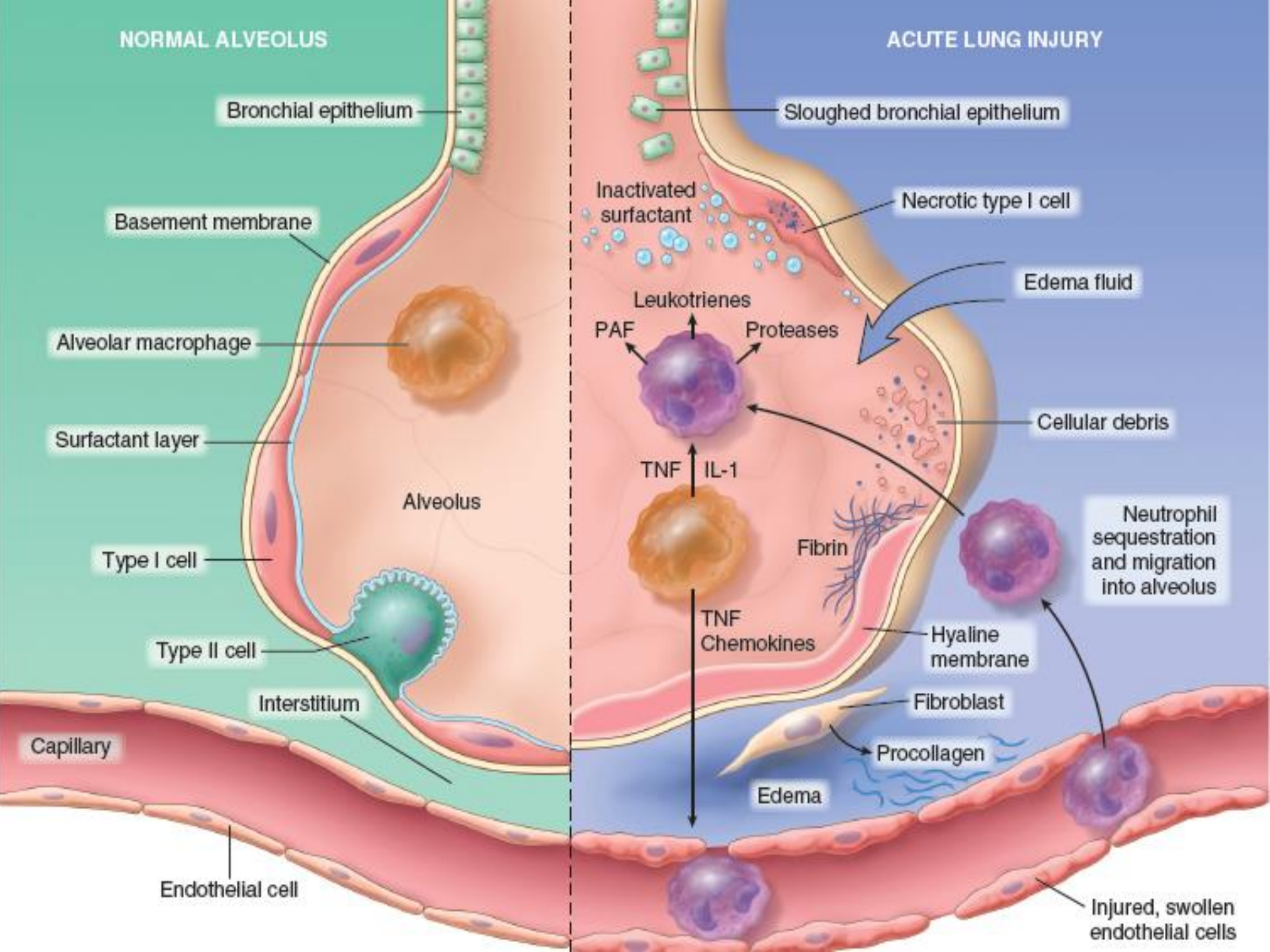
**In acute stage**, Vascular congestion, necrosis of alveolar epithelial cells, interstitial &intra-alveolar edema and hemorrhage, with collections of neutrophils in capillaries. The most characteristic finding is the presence of **hyaline membrane** (edema rich in fibrin & protein) that lines the alveoli.

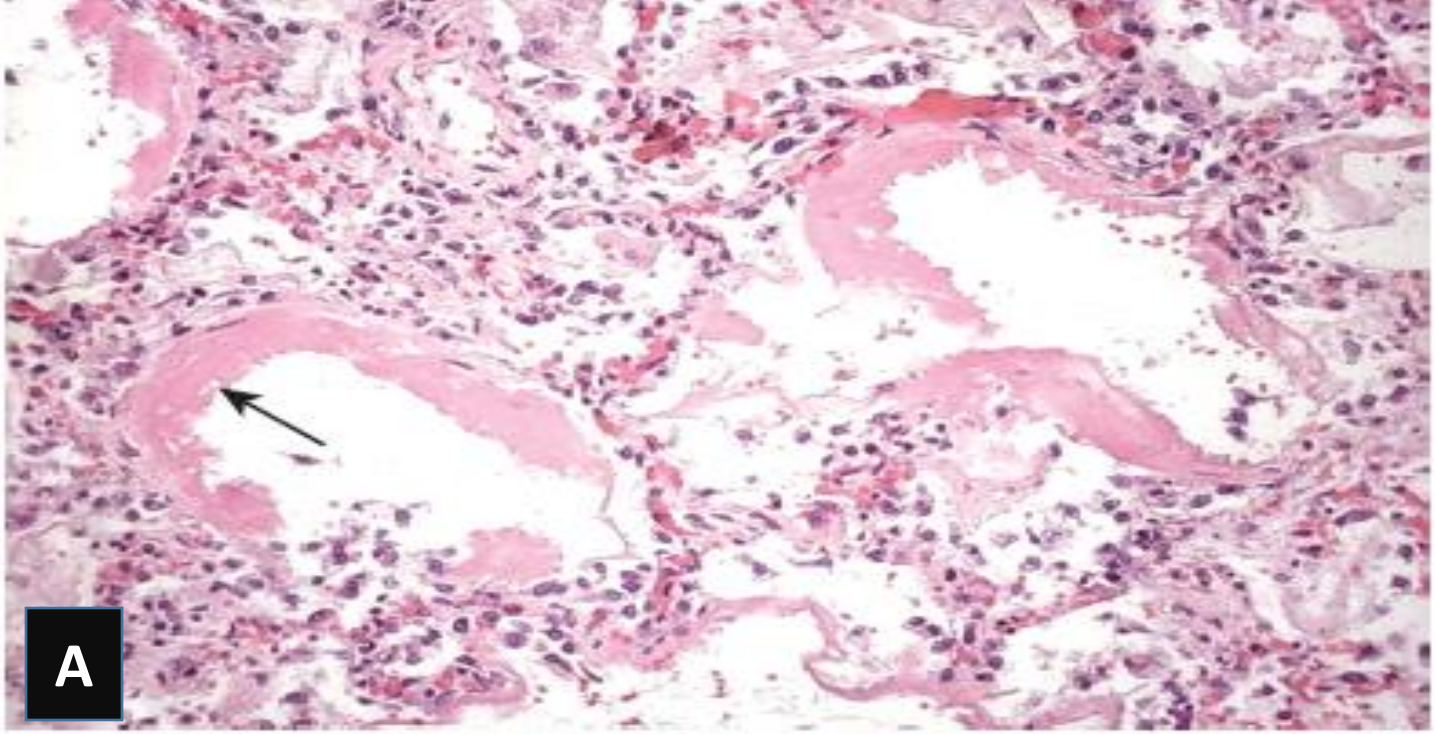
In the **organizing stage,** type II pneumocytes proliferate vigorously, and the exudate will organize into intra-alveolar fibrosis ➢ diffuse fibrosis. Unfortunately complete resolution is unusual.

**Clinical features of ARDS:**

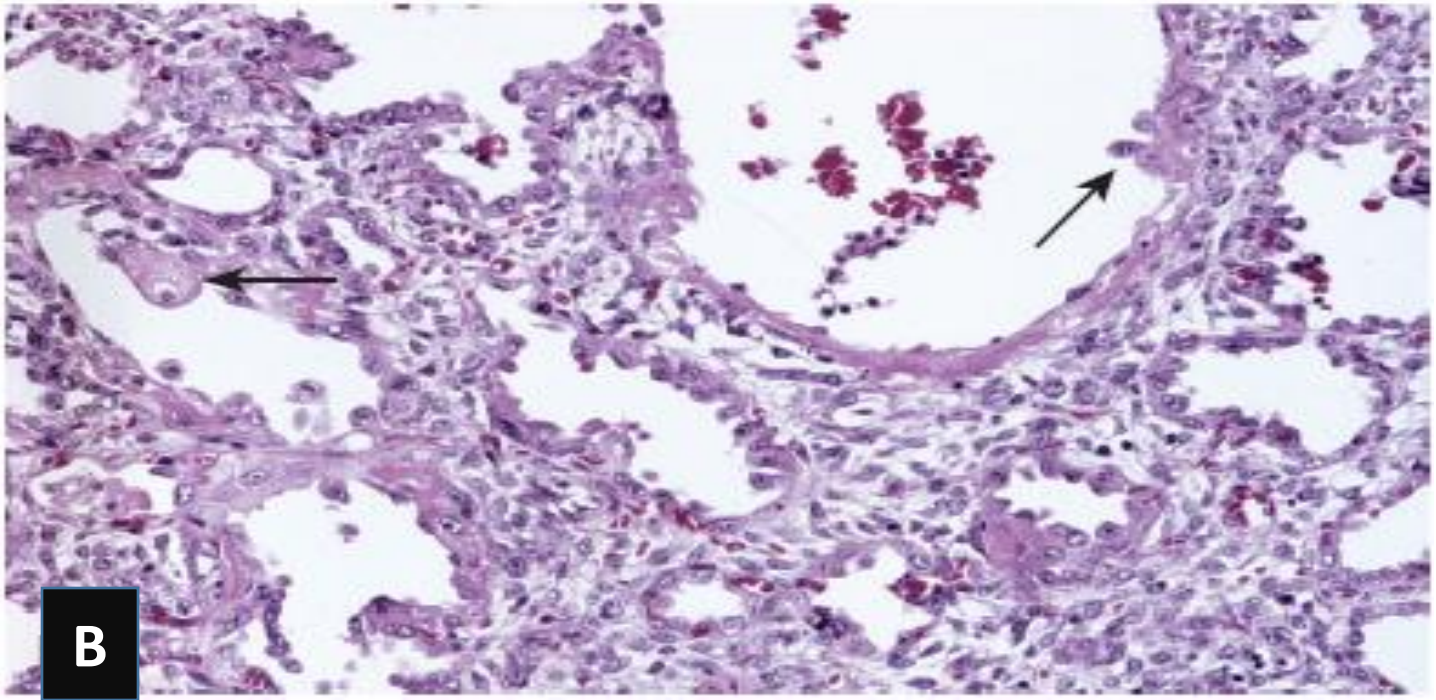
-Sudden onset of dyspnea, Cyanosis ± Resistant to O2 therapy, Bilateral diffuse pulmonary infiltrates (pulmonary edema : most common cause of non cardiogenic pulmonary edema.)

- White out on chest x-ray.


NORMAL ALVEOLUS
ACUTE LUNG INJURY
Bronchial epithelium
Sloughed bronchial epithelium
Inactivated surfactant
Necrotic type I cell
Basement membrane
Edema fluid
Leukotrienes
PAF
Proteases
Alveolar macrophage
Cellular debris
Surfactant layer
TNF
IL-1
Alveolus
Neutrophil sequestration and migration into alveolus
Fibrin
Type I cell
TNF
Chemokines
Hyaline membrane
Type II cell
Fibroblast
Interstitium
Procollagen
Capillary
Edema
Endothelial cell
Injured, swollen endothelial cells




**(A) Acute phase. Some alveoli are collapsed, while others are distended some lined by pink hyaline membranes *(arrow).***




**(B) The healing stage is marked by resorption of hyaline membranes, thickening of alveolar septa by inflammatory cells, fibroblasts, and collagen. Reactive type II pneumocytes also are seen at this stage *(arrows),* associated with regeneration and repair.**

***Outcome of ARDS:***

- High fatality in acute phase (30-50%)
- End stage fibrotic lung (20%)…HONEYCOMB LUNG → Cor Pulmonale
- Restored pulmonary ~ function (in 30%).

## II- Respiratory Distress Syndrome of Newborn

- Dyspnea & cyanosis soon after birth due to deficiency of pulmonary surfactant (produced by Pn2, mature at 36wk),so delivery before 36 wk will cause collapsed alveoli.
- Babies at risk are those from mothers with : DM,C/S, Twins
- Microscopy = to that of ARDS

# B-Chronic Interstitial Lung Diseases

Inflammation in alveolar walls with fibrosis, i & ii :

## i – Inflammation without granuloma :

1- Usual interstitial pneumonitis (idiopathic PF)

2- Environmental agents ( Asbestos, silicon… )

3- Collagen diseases (Rheumatoid arthritis, SLE)

4- Following ARDS, Radiation, Goodpasture's Syndrome, drugs…..etc.

## ii - Inflammation with granulomatous reaction :

1- Sarcoidosis.

2- Beryllium workers

3- Hypersensitivity pneumonitis.

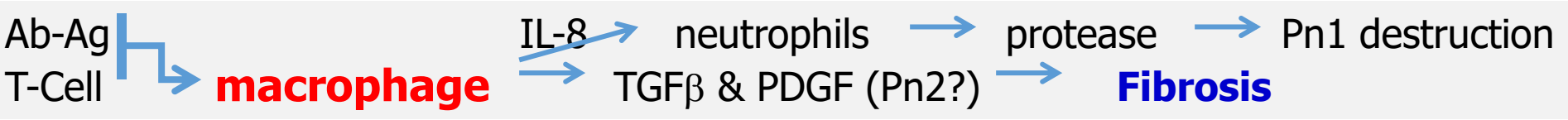
** Environmental ~ 25% , Sarcoidosis ~20% ,
Idiopathic PF ~ 15% , Collagen vascular dz ~10%.
-Remaining 30% : >100 causes.

# Usual Interstitial Pneumonitis ( Idiopathic PF)

- M > F , most >60.
- Diagnosed after exclusion of other causes(because histology ~ other dz, like connective T. dz, silicosis..)
- ~ +ve autoantibodies & certain types of immune complexes in serum.

**Pathogenesis** :

Immune complex or T cell-activated macrophages secrete mediators like IL-8 which attracts neutrophils that in turn release proteases, these proteases will injure pneumocytes-I, also macrophage (? + Pncytes-II) will secrete TGFβ & PDGF → Fibroblast→ interstitial fibrosis.

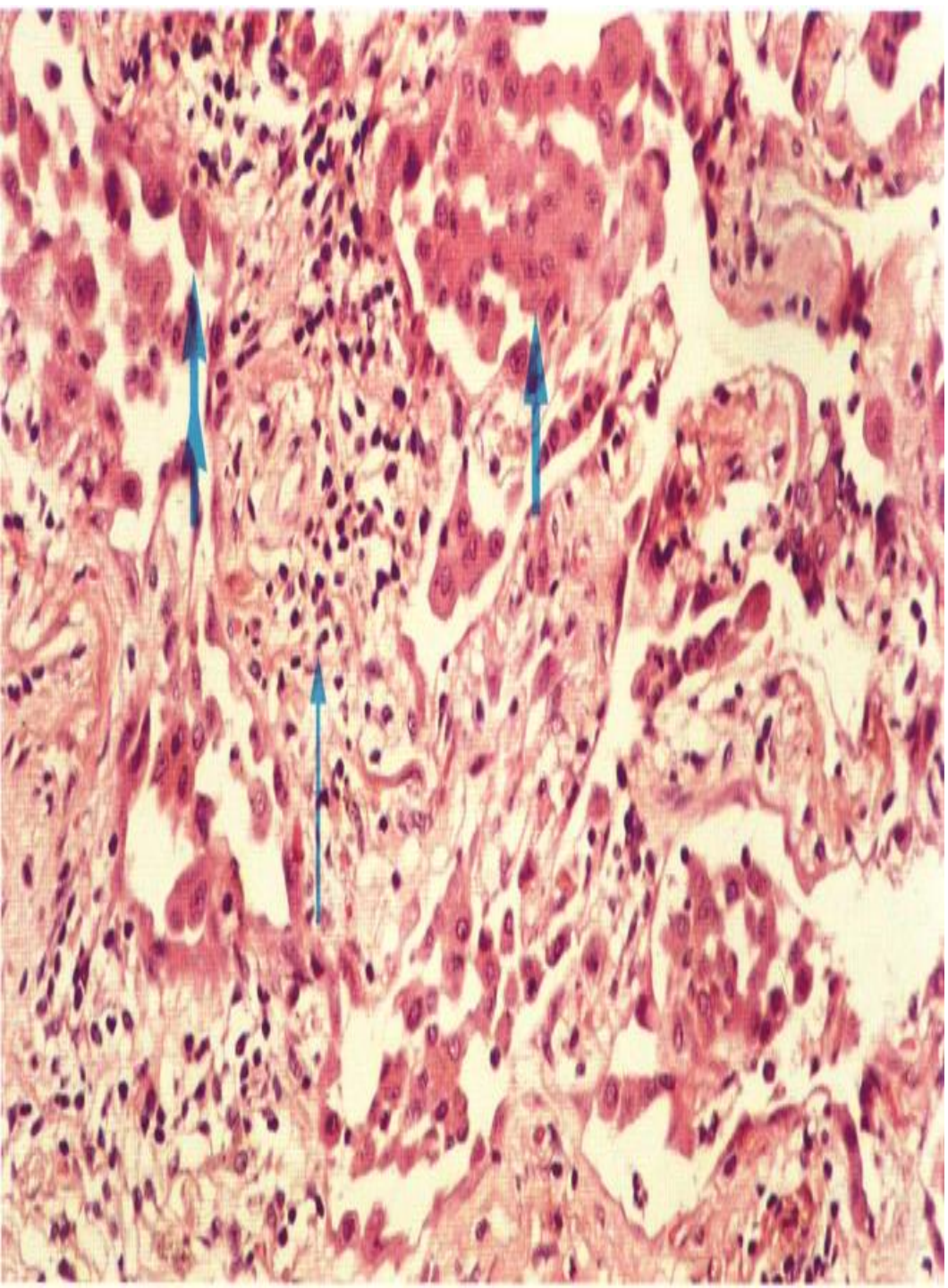


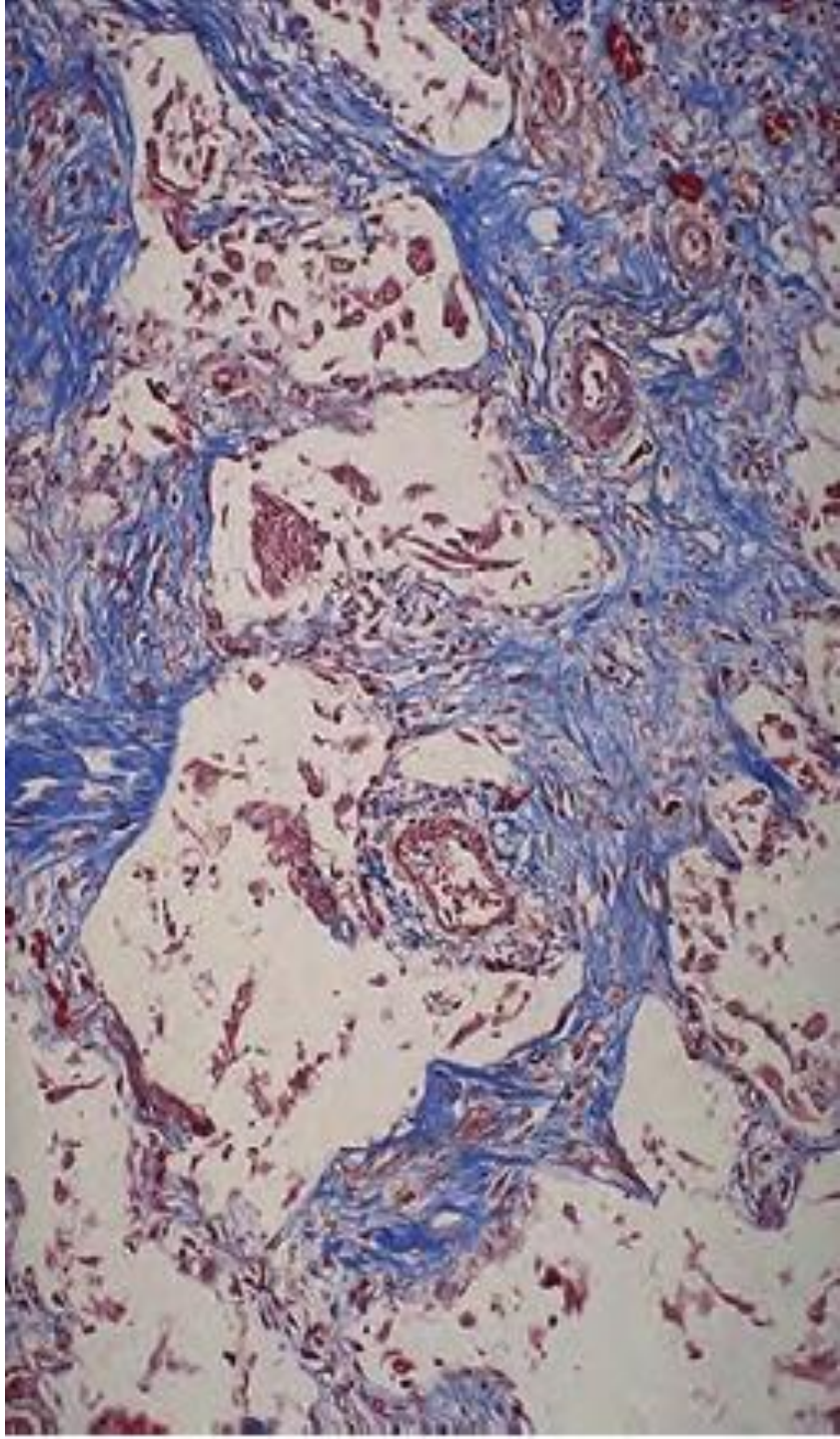
*Microscopy of* **(UIP/IPF)**:

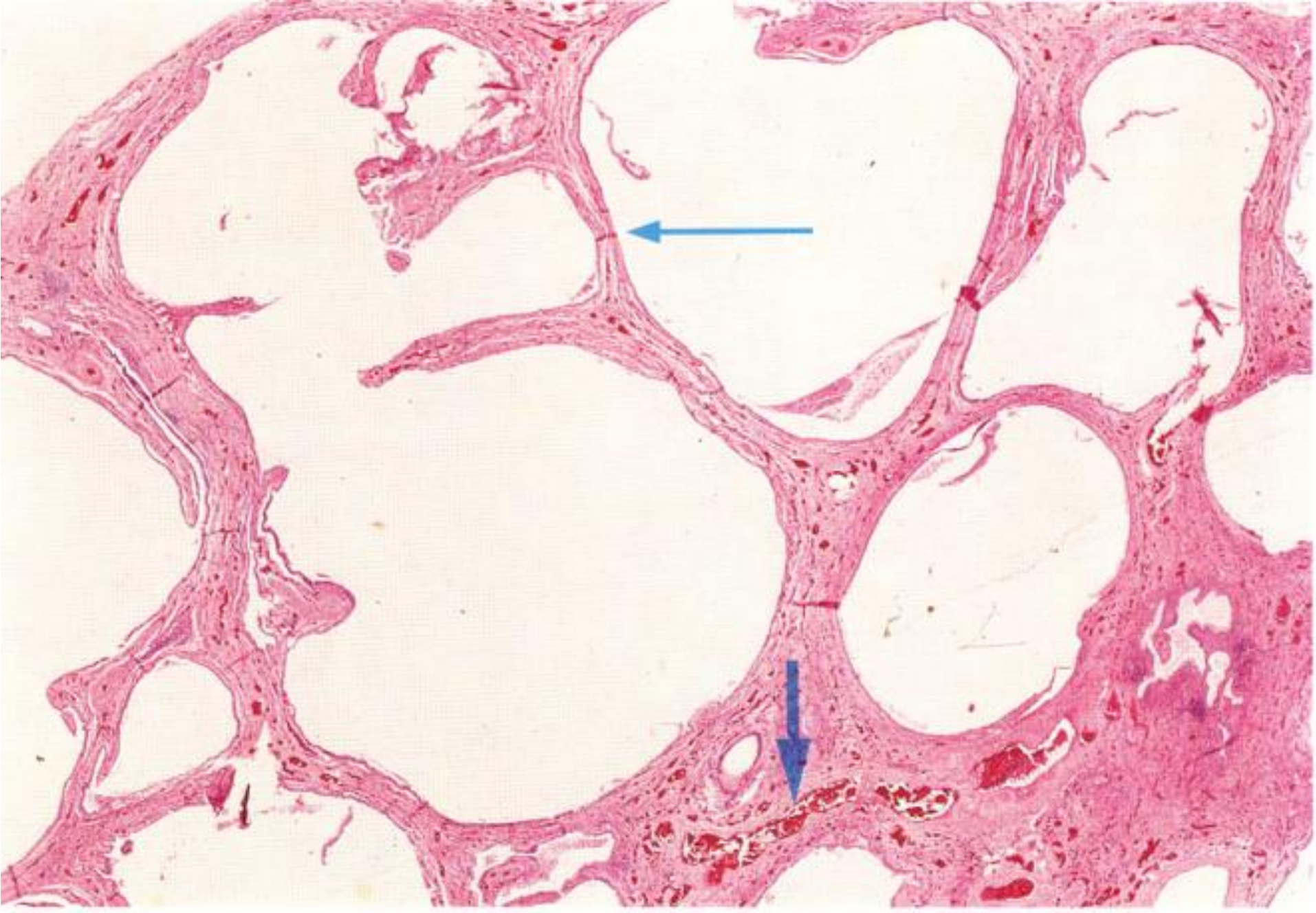
- Chronic inflammation & fibrosis in alveolar wall.
- Destruction of pneumocytes type I
- Proliferation of pneumocytes type II
- No granuloma
- Not all areas affected equally
- Usually more in peripheral areas
- Patchy fibrosis→ Honeycomb lung

***DX***:

- Clinical : Insidious onset of non-productive cough, dyspnea , cyanosis, cor pulmonale , death within ~3yrs.
- Chest X-ray : Bilateral ground glass opacities
- Lung biopsy: above (not specific).







**Interstitial fibrosis in Honeycomb lung**

# Honey comb Lung

## Hypersensitivity Pneumonitis (allergic alveolitis)

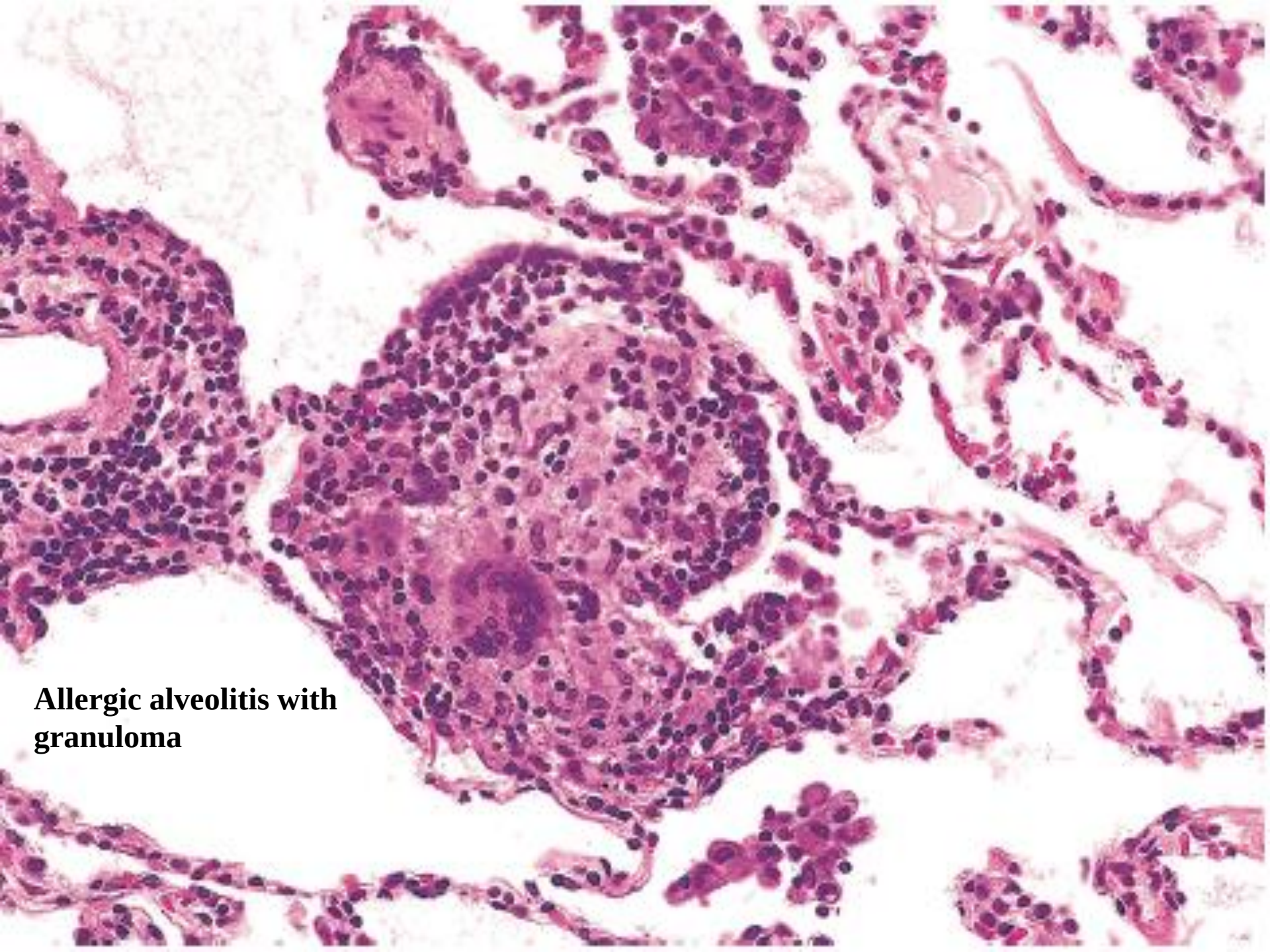
- Immunologically mediated interstitial disease.
- Prolonged exposure to organic dust.
- Antigens include fungal or bacterial spores, animal protein… etc
    - * Farmer's Lung -- Spores of Actinomycetes
    - * Pigeon fancier's lung -- Bird droppings
    - * Coffee worker's lung -- Coffee been dust.

***Phases of Hypersensitivity Pneumonitis :***

- Acute : direct irritant effect $\rightarrow$ fever , cough & dyspnea.
- Chronic : delayed hypersensitivity reaction.

**Pathology**:

Non caseating granuloma in alveolar walls + FIBROSIS


Allergic alveolitis with
granuloma

# Lower respiratory tract

## Lung infections

Respiratory tract infections are more frequent than infections of any other organ ; because:

1-Lung is constantly exposed to contaminated air,

2-Nasopharyngeal flora are regularly aspirated even by healthy persons.

3-Some common lung diseases render the lung vulnerable to infections.

***Pneumonia:*** Is infection of lung parenchyma.

***Presentation*****:** Cough , sputum , fever , chest pain.

***Dx*** :- History, Examination, Chest X ray, Blood picture…

* Isolation of microbe from:(sputum, blood, pleural fluid Or lung bx)
* serology.

**Classification** of pneumonias Either by :

A-Etiological agent (e.g. staph. Pn, strep. P, Klebsiella pn), or by

B-Clinical setting in which the infection occurs as :-

**-Community-acquired acute pn** (streptococcus Pn, H.influenzae pn..)

**-Community-acquired atypical pn**. (Mycoplasma, Chlamydia ,viral…)

**-Hospital-acquired (nosocomial) pn**.(Klebsiella , E.Coli .or staph pn.)

**-Aspiration pn**. (anaerobic oral flora),

**-Chronic Pn**. (TB, Fungal ,Nocardia..).

**-Pneumonia in immunocompromised** pt (P. carini,M. avium)

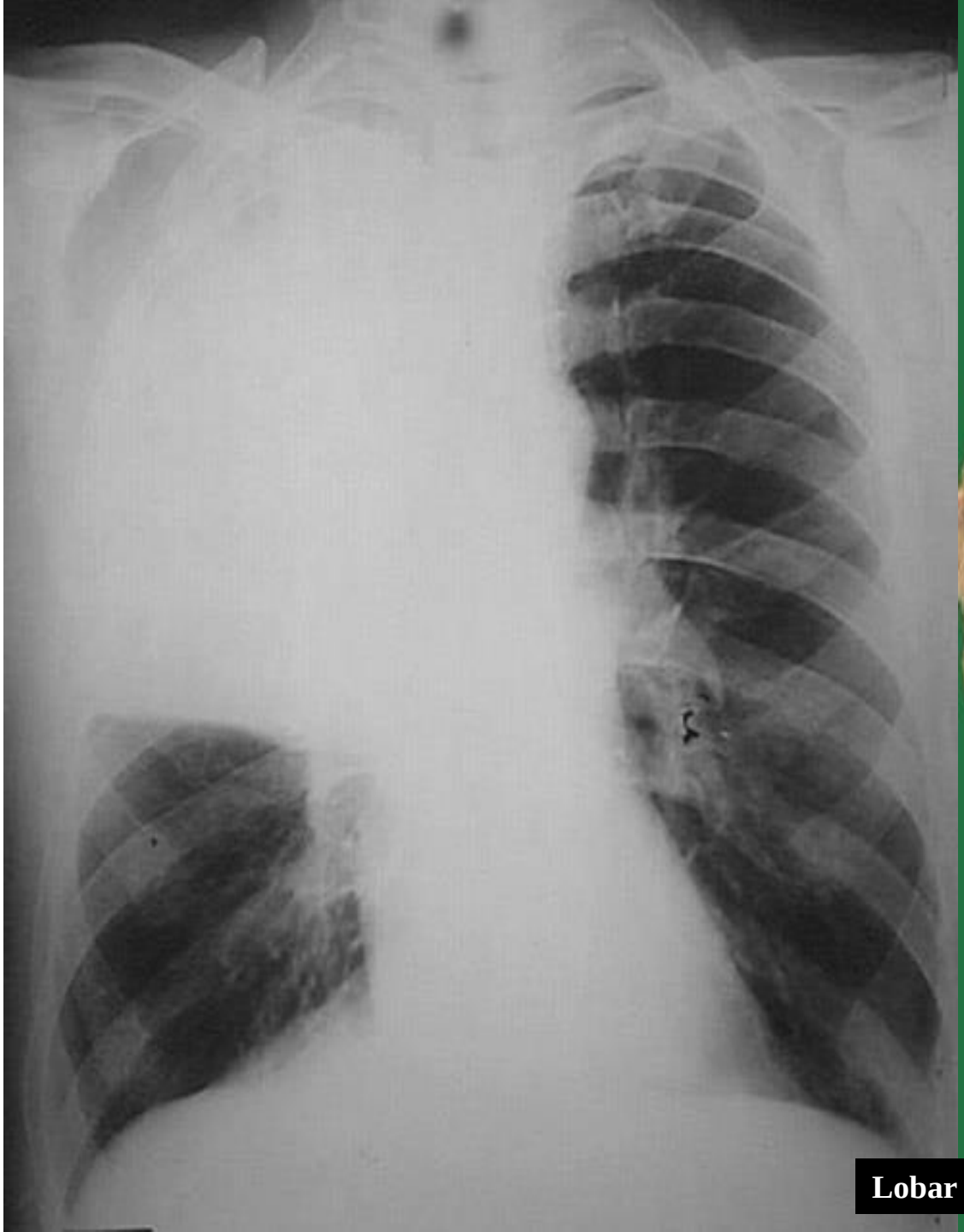
According to **anatomical** (X-ray) pattern, Pn can be described as:

1-***Lobar Pn:*** Whole lobe of the lung is involved by inflammation.

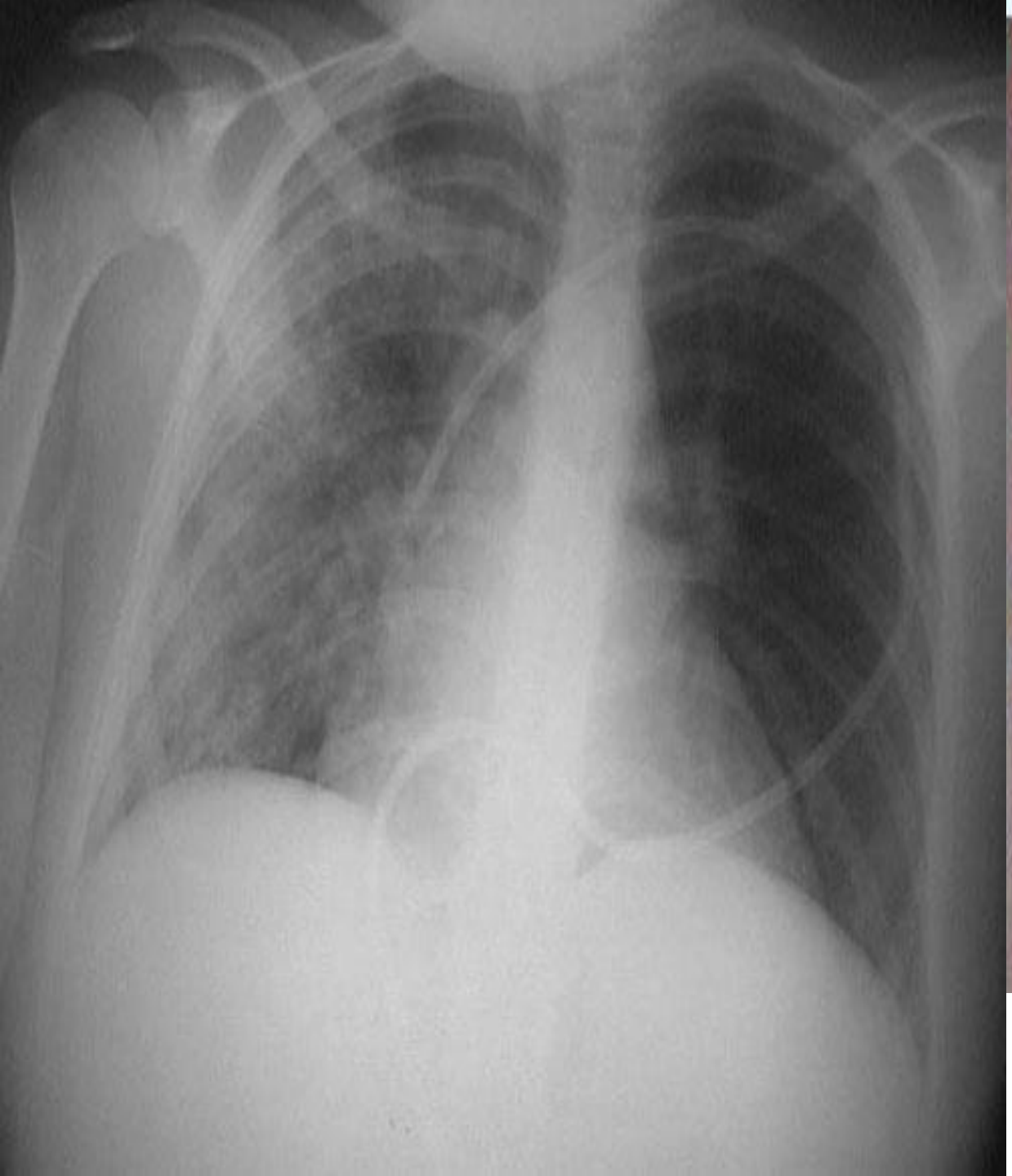
2-***Bronchopneumonia*** *:* Inflammation is patchy & bronchocentric.

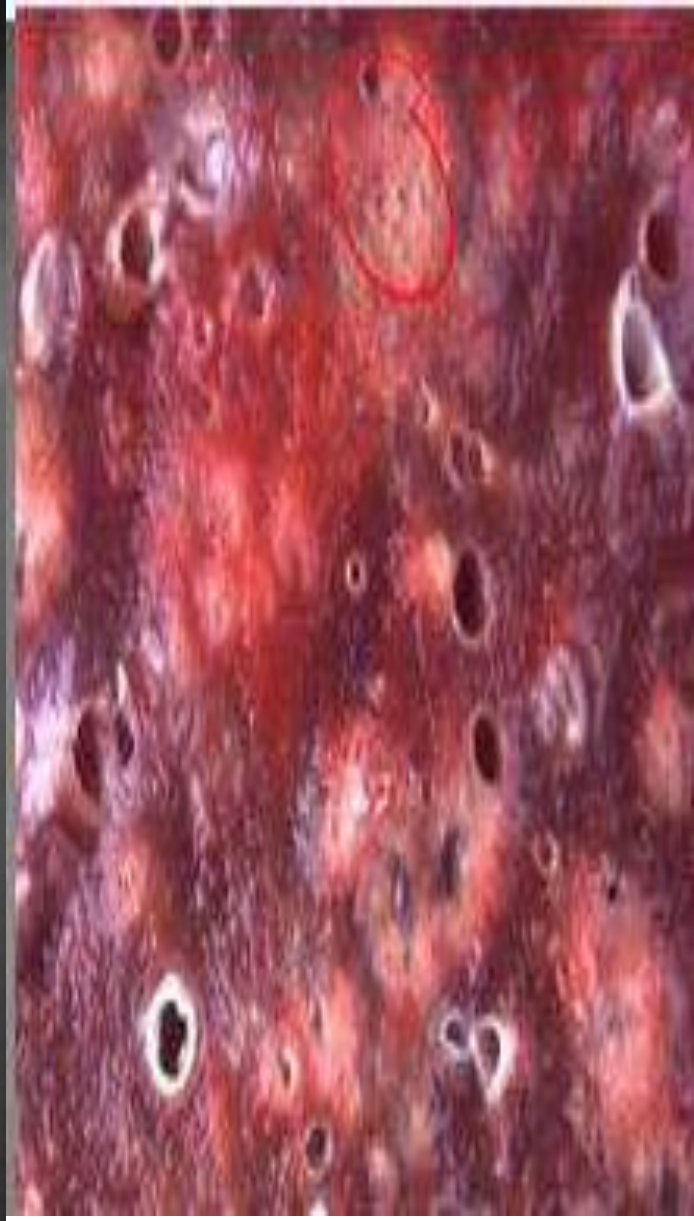
3-***Interstitial Pn:*** Inflammation involves the alveolar walls with almost empty alveolar space.

**Acute Bacterial pneumonia,** In general characterized by formation of **CONSOLIDATION (solidification**) which is defined as hardening of lung parenchyma due to presence of exudate in alveolar spaces.



Lobar Peumonia





**Bronchopneumonia**

# *A- LOBAR PNEUMONIA*

- Community acquired Pn.
- Streptococcal Pn is the cause in $\geq$ 90 % of cases.
- Usually affects healthy of any age
- More in pt with predisposing conditions e.g. COLD, Heart failure…
- Presented as acute onset of fever, cough, rust colored sputum & chest pain.

**- Pathology:**

Usually affects the lower lobes and passes into 4 stages:

*- CONGESTION 1-2 days*

*- RED HEPATIZATION 2-4 days*

*- GREY HEPATIZATION 4-8 days*

*- RESOLUTION 8-9 days.*

** these stage are modified by treatment.*

## 1- Congestion:

- Heavy red lungs (due to severe vascular congestion)
- Intra alveolar exudate with few neutrophils
- Bacteria +++

* Clinical : fine crepitation with watery sputum.

## 2- Red hepatization:

- Firm airless , liver-like lung
- Fibrinopurulent pleuritis
- Intra-alveolar exudate : organisms + cells + erythrocytes + neutrophils + fibrin.

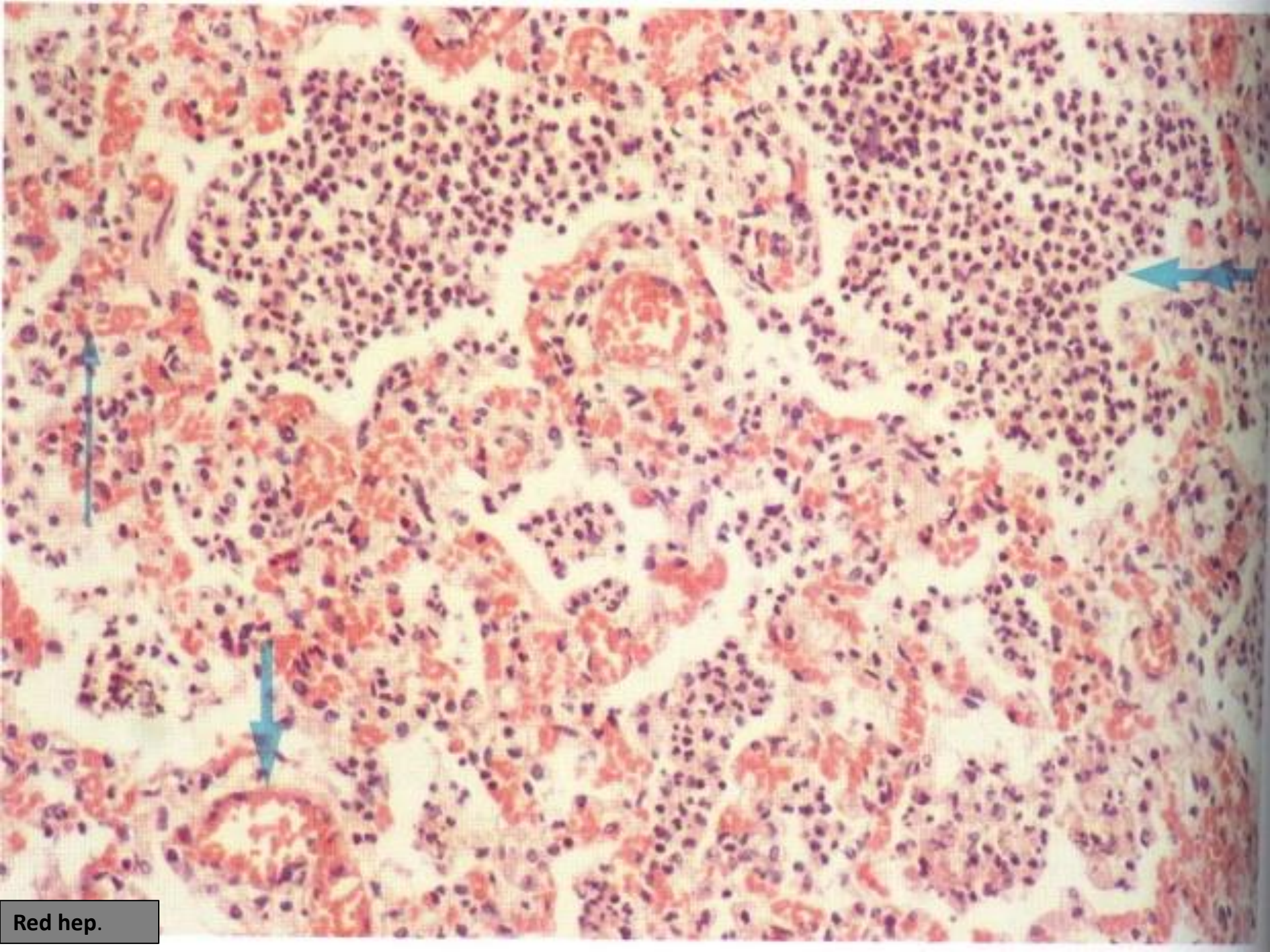
*Clinical : Bronchial breathing + rusty sputum

## 3- Grey hepatization :

- Disintegration of RBC's.
- Increased intra alveolar fibrin & macrophages.
- Dry grey brown cut surface

## 4-Resolutionon:

Enzymatic digestion of exudate →ingested by phagocytosis , sometimes with residual adhesion



Red hep.

# Pathology of the Respiratory System-5

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