



Pathology of the Respiratory System-5

DR. ARKAN O. AL-ESAWI
J.B.H , H.S.D.P , M.B CH.B.

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

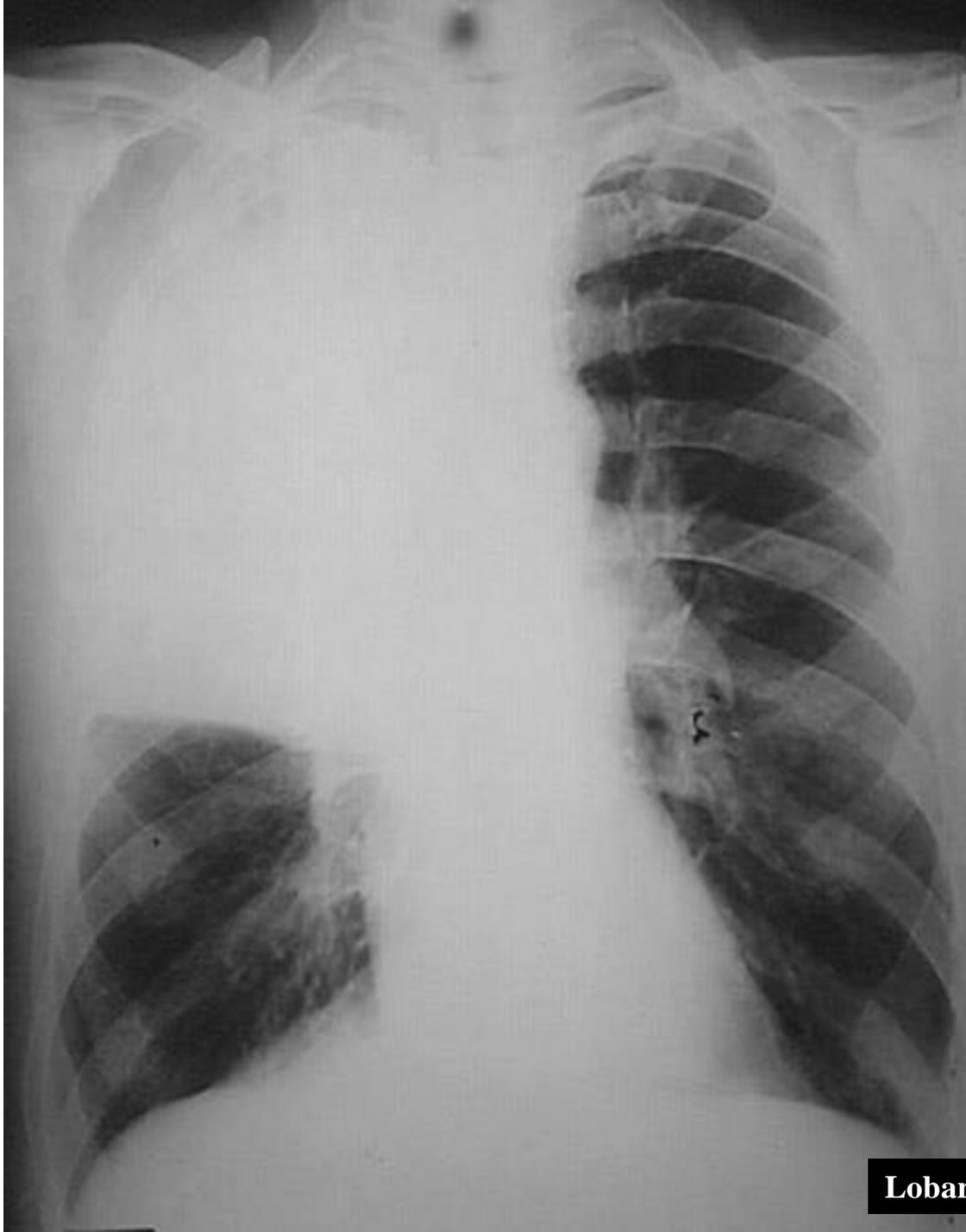
B-Clinical setting in which the infection occurs as :-

- 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)

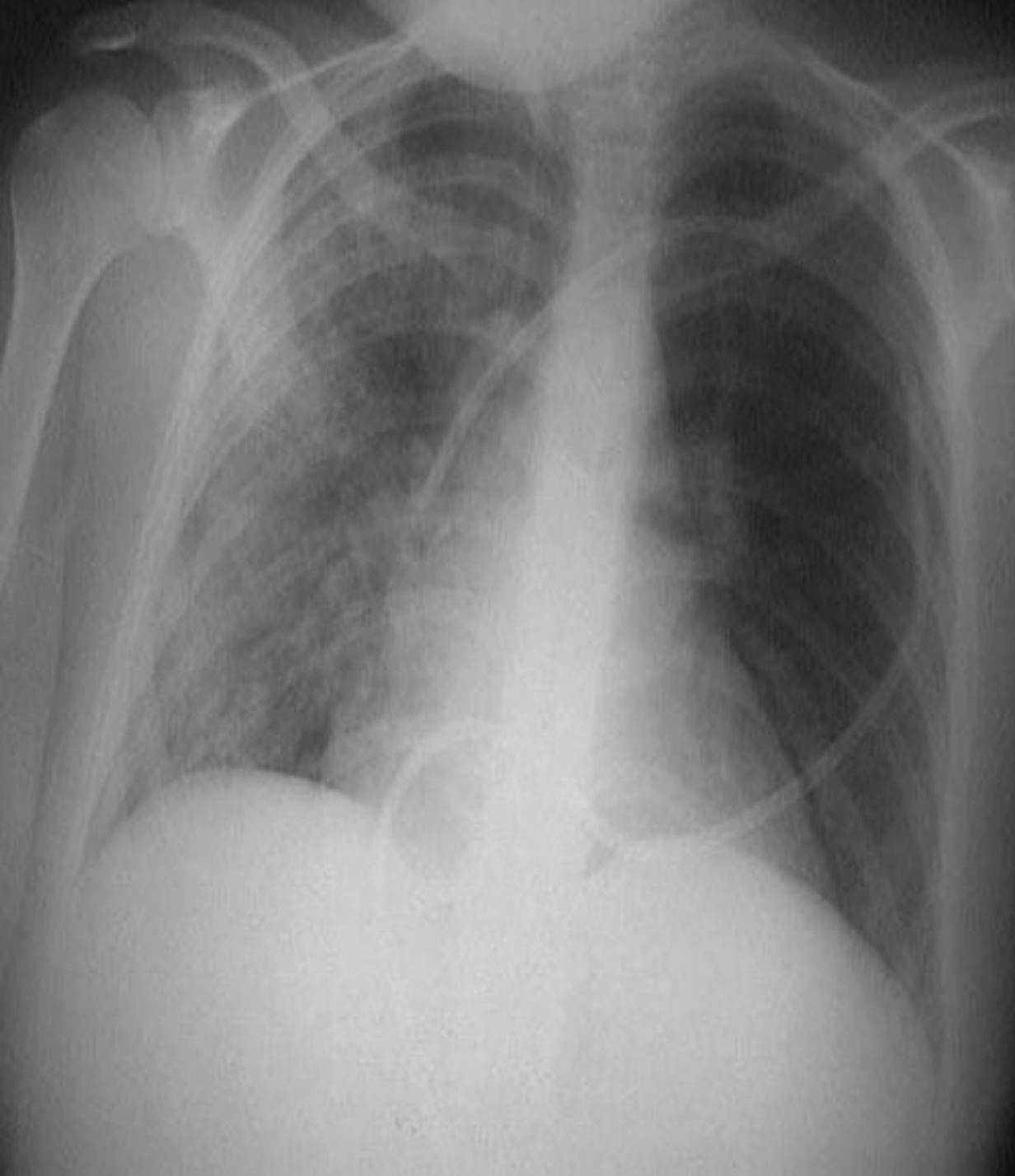
According to **anatomical (X-ray) pattern**, Pn can be described as:

- 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 ≥ 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:

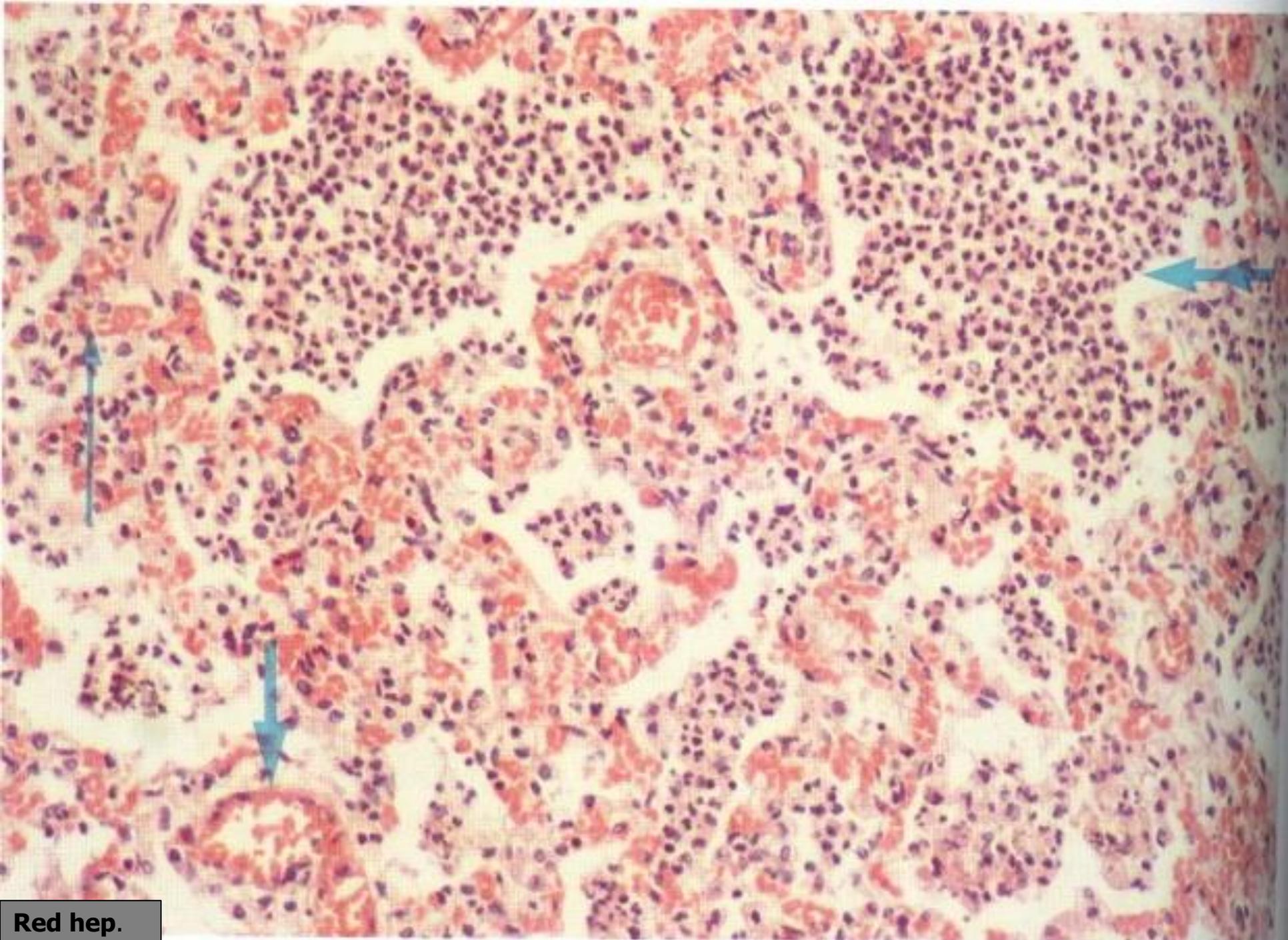
- Firm airless , liver-like lung
 - Fibrinopurulent pleuritis
 - Intra-alveolar exudate : organisms + cells + erythrocytes + neutrophils + fibrin.
- *Clinical : Bronchial breathing + rusty sputum

3- Grey hepatization :

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

4-Resolution:

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



Red hep.

B- BRONCHOPNEUMONIA

- Increased in elderly , infants (extreme age)
- Inflammation of conducting airways with local intra-alveolar spread → patchy consolidation
- Usually multilobar, bilateral and basal.
- More destructive with more complications.
- Pleura less likely involved.
- Bacteria :staph,strep, haemophilus, pseudomonas spp.... Etc.

Characteristics of Common bacterial pneumonias:

- *Pneumococcal pneumonia* most common cause of community acquired pn. (flora in 20%,...? culture from sputum , blood is more specific.....) .
- *H.influenzae pneumonia* :us. follows viral infection in children, most common bacterial cause of COPD exacerbation.

- Klebsiella pneumonia: bronchopneumonia or lobar.
Gelatinous sputum (cap. polysaccharides) → difficulty coughing up. (↑ complications: Non-resolution, abscess & fistulae)
↑ in patients with COPD, alcoholics, old, malnourishment.
- Staphylococcal pneumonia :
 - Severe abscessing broncho Pn.
 - Most common cause of secondary pneumonia (pneumonia superimposed on viral)
 - Associated with upper respiratory tract infection.
 - More common in IV drug addicts, in hospitalized pt & in adults with COPD.

- Pseudomonas aeruginosa pneumonia :

Usually hospital acquired severe bronchopneumonia

Pts. at risk are those with cystic fibrosis & Immunosuppressed Pt.

- Pathology : abscess formation & empyema , with

prominent vascular invasion → vasculitis + necrosis (*Necrotizing Pneumonia*)

- Very high mortality.

- Moraxella catarrhalis : 2nd most common bacterial cause of acute exacerbation of COPD and it is the 3rd common cause of otitis media (others: S.pneum and H.influnz).

- Legionella Pneumonia :

Intracellular organism visualized by silver stain, Acquired through contaminated water cooled air conditioning system ,or hospital acquire.

-Aspiration Pneumonia

- Aspiration from :

- Oropharyngeal secretion
- Gastric contents
- Mixture of food and fluid.

- In debilitated patient ,Pt with depressed sensation (abnormal gag-reflex) e.g. post anesthesia & paralyzed pt.
- Mixed bacterial infection + Chemical (acid) damage +consolidation

Result : Severe Necrotizing Pneumonia

Complications of bacterial pneumonias :

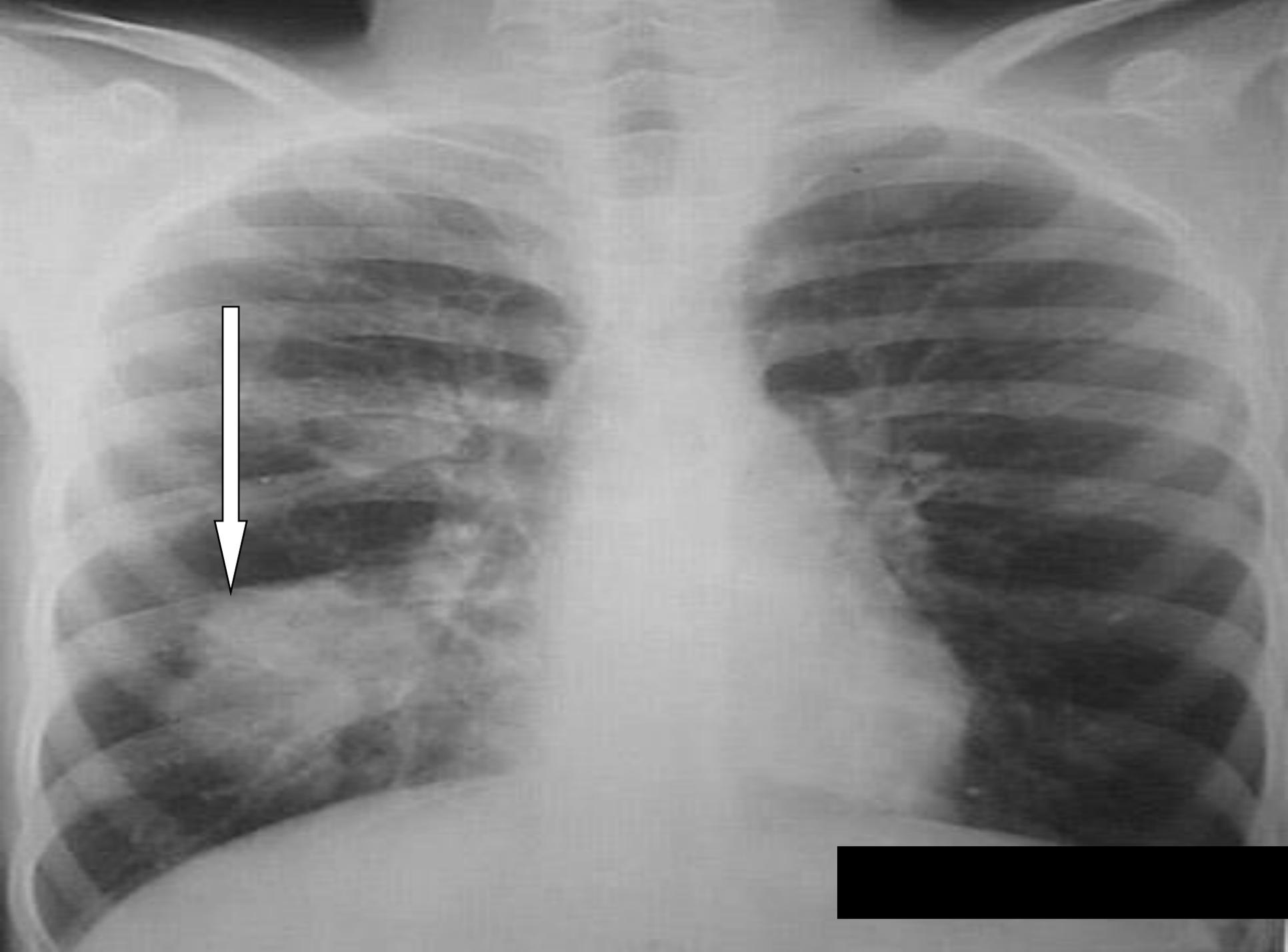
- 1- **Non resolution and organization** of exudate leading to fibrosis.
- 2- **Abscess formation** due to tissue destruction necrosis & suppuration.
- 3- **Bacteremic dissemination** → meningitis, arthritis, infective E carditis.
- 4- **Pleural involvement** :
 - Pleural effusion .
 - Empyema due to accumulation of pus in pleural cavity \pm adhesions.
 - Fistula formation.

Lung abscess

- Localized area of suppuration within the lung

- Pathogenesis:

- 1- Aspiration of infective material (alcohol , coma..)
- 2- Post pneumonic(staph, S.pneu and klebsiel)
- 3- Bronchial obstruction(e.g due to tumor)
- 4- Infection in existing cavities or cysts(~ TB..)
- 5- Septic embolism.
- 6- Bacteraemic seeding from adjacent focus.



Morphology of abscess :

-Variable size , may be single or multiple , depending on mode of development.

* **Aspiration** : Usually solitary , more in RL

* **Postpneumonic** : Usually multiple , more basal.

* **Hematogenous**: Usually multiple & any site

- Culture of pus - often mixed aerobic / anaerobic.

Histology:

Focus of suppuration surrounded by fibrous wall and containing mixed chronic inflammatory cells.

Fate & complications of lung abscess:

- 1- Healing by fibrosis leaving a sterile cavity.
- 2- Rupture with partial drainage of contents :-
 - *Radiological picture → *Air-Fluid* level
 - *Rupture into pleura → *Empyema*
 - *Rupture into bronchus → *Bronchopneumonia*.
- 3- Formation bronchopleural fistula → *Pneumothorax*.
- 4- Septic emboli(~ to CNS ,Kidney.....)
- 5- Lung hemorrhage from vessels in or near the fibrous wall .

C- INTERSTITIAL (Atypical) PNEUMONIA

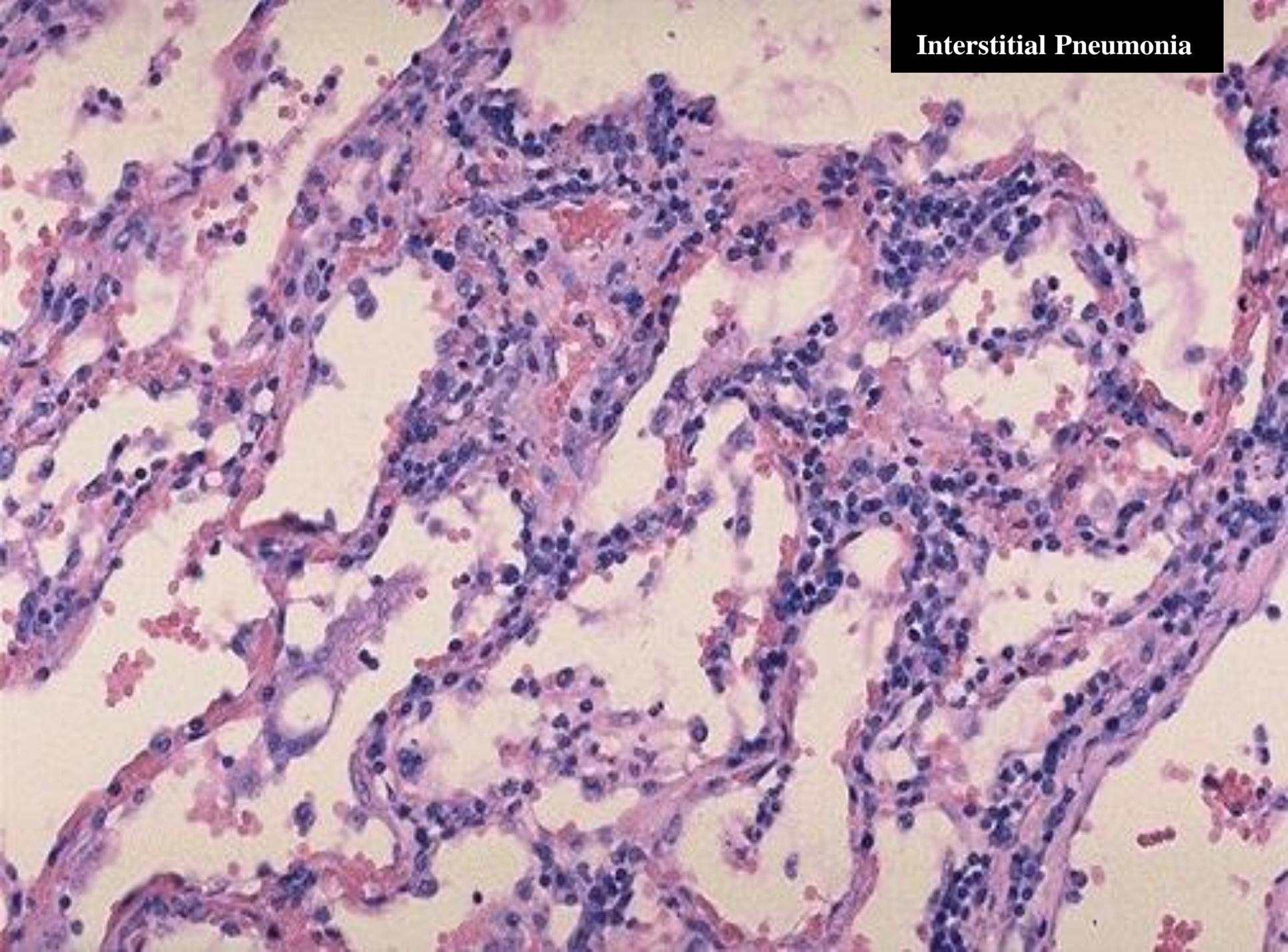
A group of pneumonias(Pneumonitis) caused by nonbacterial agents including :

- Mycoplasma (Most common cause of atypical pneumonia)
- Chlamydia and Rickettsiae
- Viruses -Resp.syncytial v, parainfluenza, measles....
- RSV: Most common cause of pneumonia in infants

Features :

- Usually community acquired
- Follows upper respiratory infection and when the inflammation extends to the alveoli it will cause interstitial inflammation of lung.
- The inflammatory reaction is patchy or lobar,in the alveolar walls (not in spaces) and it is Lymphocytic .

Interstitial Pneumonia



Clinical picture of atypical pn:

Insidious onset, minimal cough ,minimal expektoration, mild \uparrow WBC's ,
no Consolidation.

- Radiological picture : Transient ill defined patches, mainly in lower lobes.
- They call it atypical because clinically and radiologically differs from usual bacterial Pn.
- In case of viruses , viral inclusions may be seen.
- In mycoplasma: cold agglutinin present.
- Severe cases may progress to Diffuse Alveolar Damage with formation of hyaline membranes.

CHRONIC PNEUMONIAS

1- Tuberculosis

- Communicable disease caused by *M. hominis* , *bovis*, *avium*,...etc.
- May affect any organ but the lung is the most affected organ.
- Route of infections : Inhalation → Lung or Ingestion (Milk *M. bovis*)→ Intestine.
- Not all exposed get infection.
- Mostly self limited (\pm viable organisms).
- \uparrow risk in DM ,silicosis, Hodgkin's, AIDS...etc.

pathogenesis :

-Virulent strains prevent fusion of phagosomes-containing bacilli to lysosomes and prevent the ingestion (of bacilli) by lysosomal enzymes (through inhibition of calcium signals and blocking assembly of proteins for phagolysosomes fusion), So bacilli will proliferate inside macrophage; but 3wk later T-helper cells will activate these macrophages by gamma IFN (CMI) to be immune competent against the bacilli through active phagolysosome that exposes bacilli to inhospitable acidic media. Also active macrophages will produce (NO) that generates active **free radicals** able to destruct several mycobacterium Ag. And this will control 95%(healing) of TB infection.

-Development of CMI is important in immunity and resistance to TB bacilli (inhibit/kill) but hypersensitivity reaction can also cause tissue destruction (by granuloma \pm caseous necrosis). The predominates (protective or destructive response) will determine whether primary focus of infection remains localized or disabling dz appears.

*All diseased pts are infected (& can transmit infection) but not all infected are diseased.

A-Primary TB

Infection in unsensitized person; appears as ~ as flu-like illness.

But elder and immun. persons may lose their sensitivity to bacilli and so will develop more than one primary TB.

- Morphology :

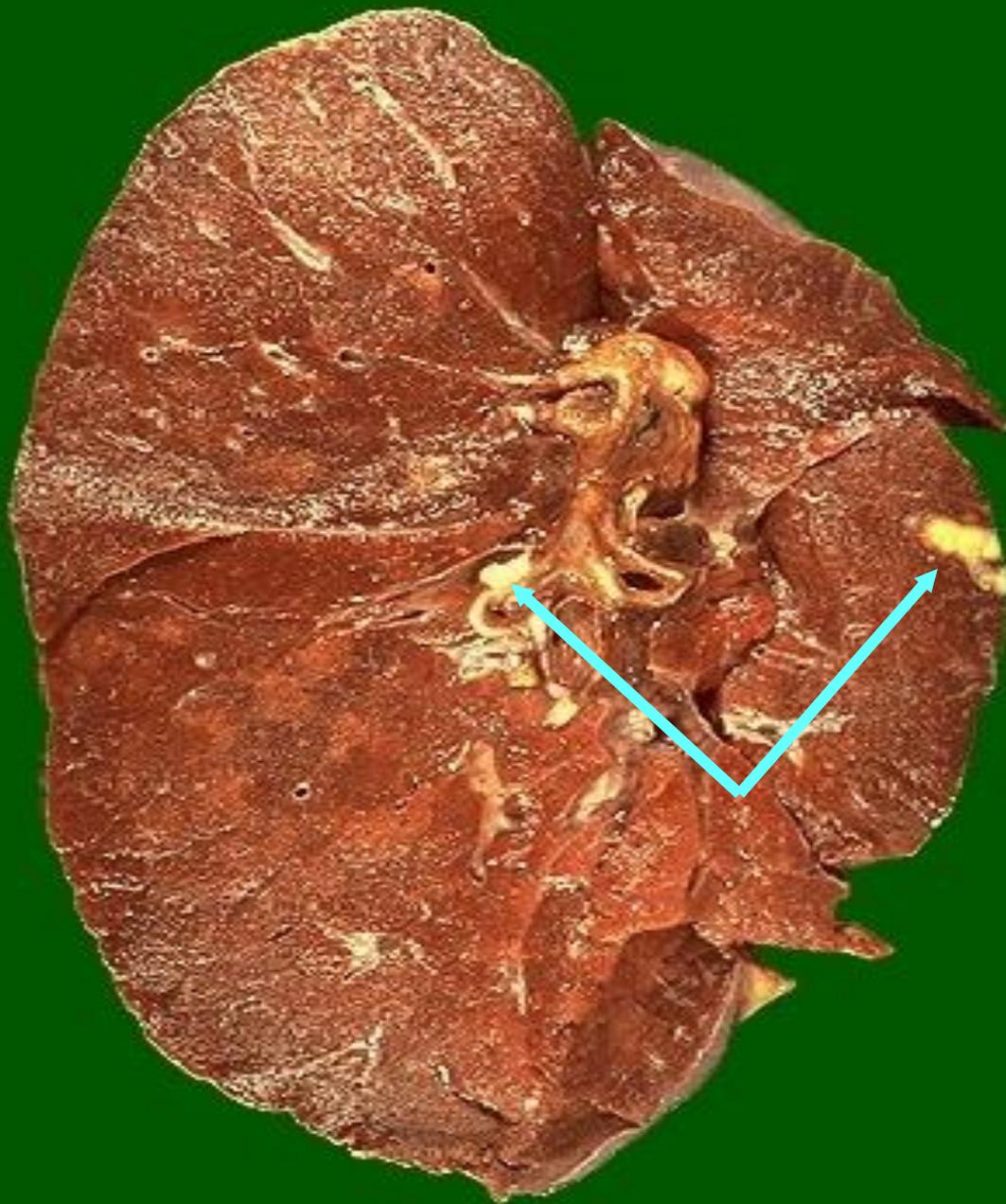
Caseating granuloma: Caseation surrounded by chronic inflammatory cells, epitheloid macrophages, Langhan's giant cells, fibroblasts...)

*The initial subpleural (us.lower lobes)lesion called ***Ghon focus***, and when there is enlarged hilar LNs it will form ***Ghon Complex*** (= Ghon focus + nodal involvement).

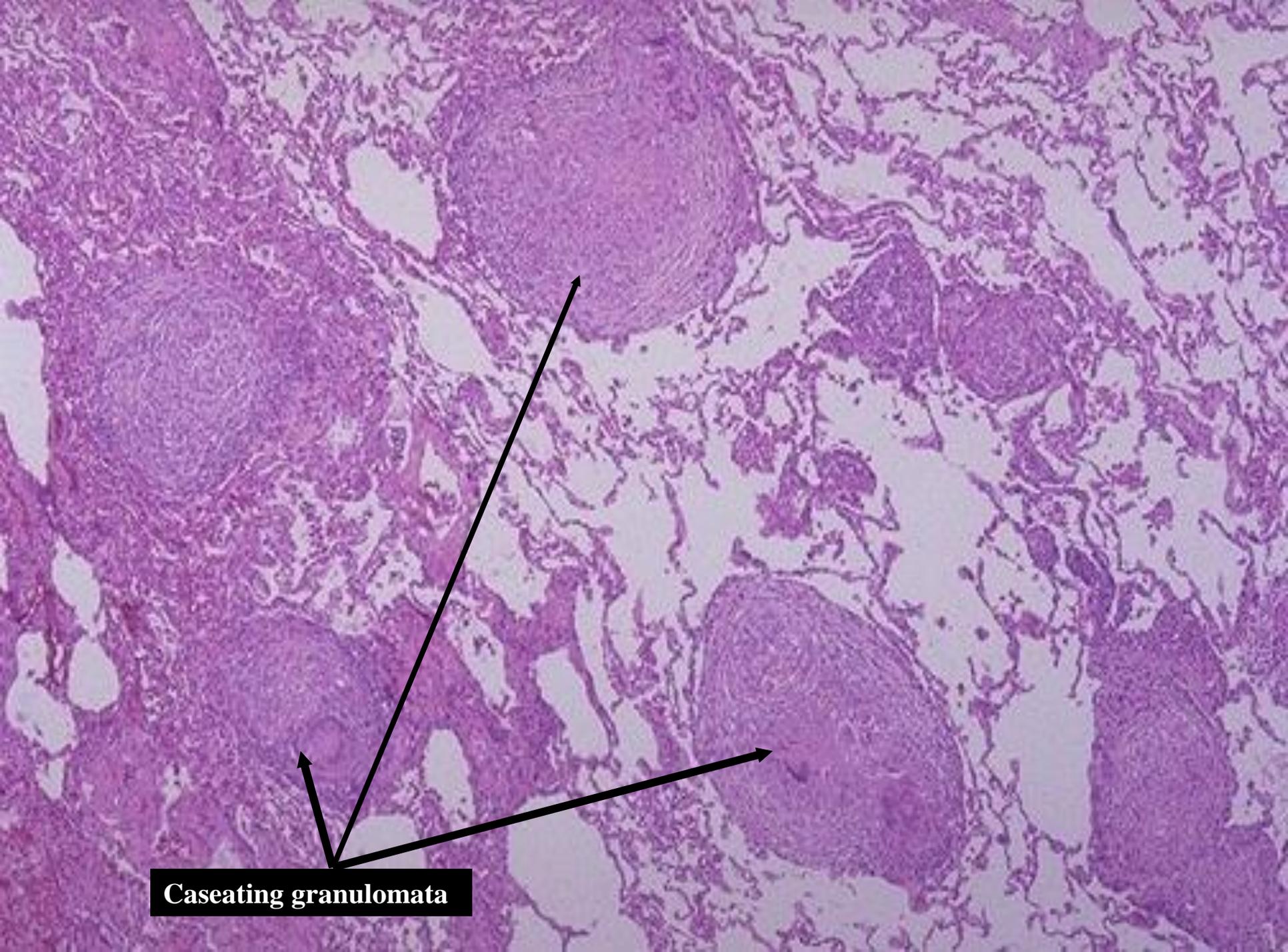
Outcome of Primary TB :

In 95% cell mediated immunity→ healing in 3 weeks by fibrosis ± Ca+.

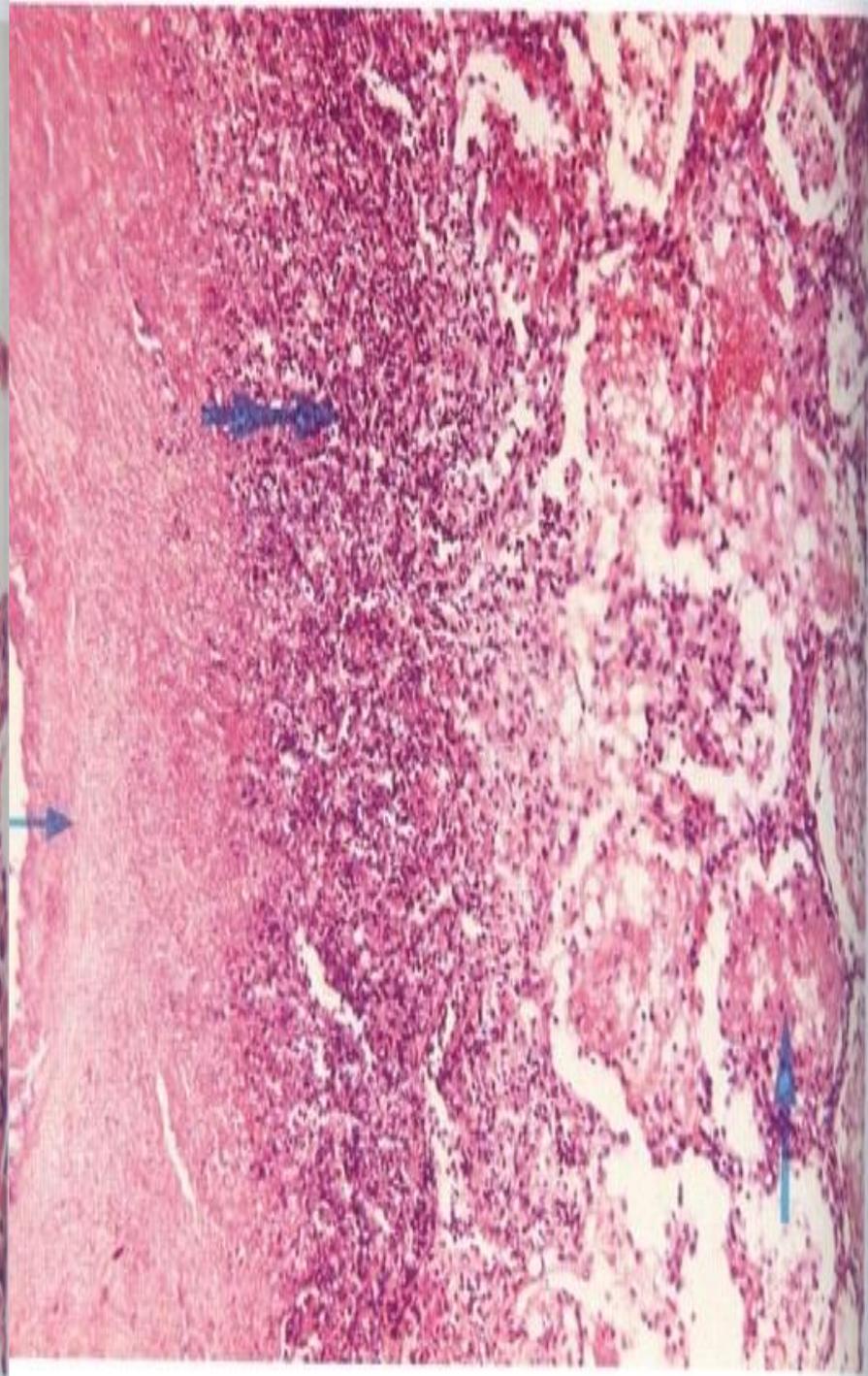
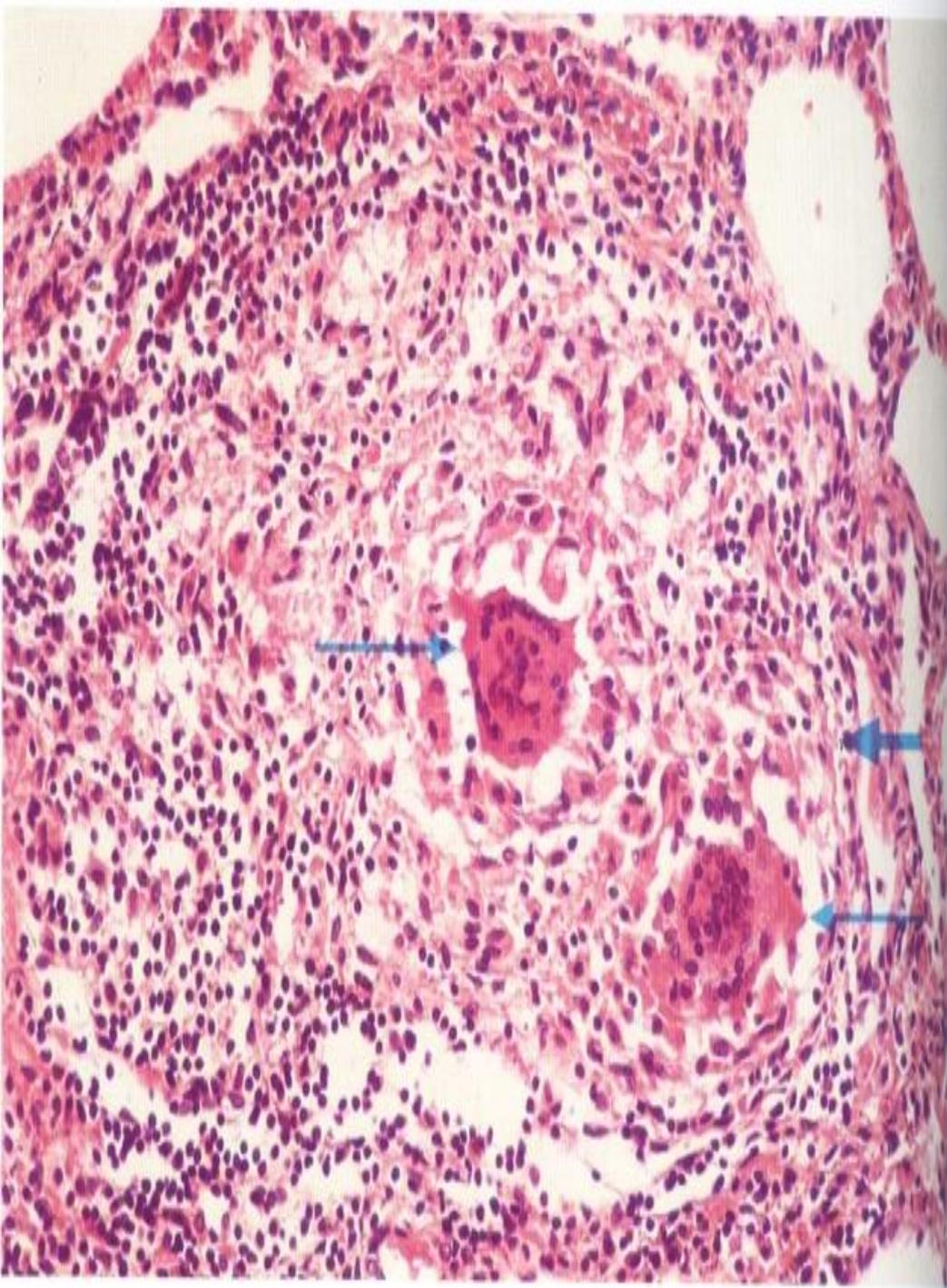
Uncommonly disseminated disease (***Progressive Primary TB***).

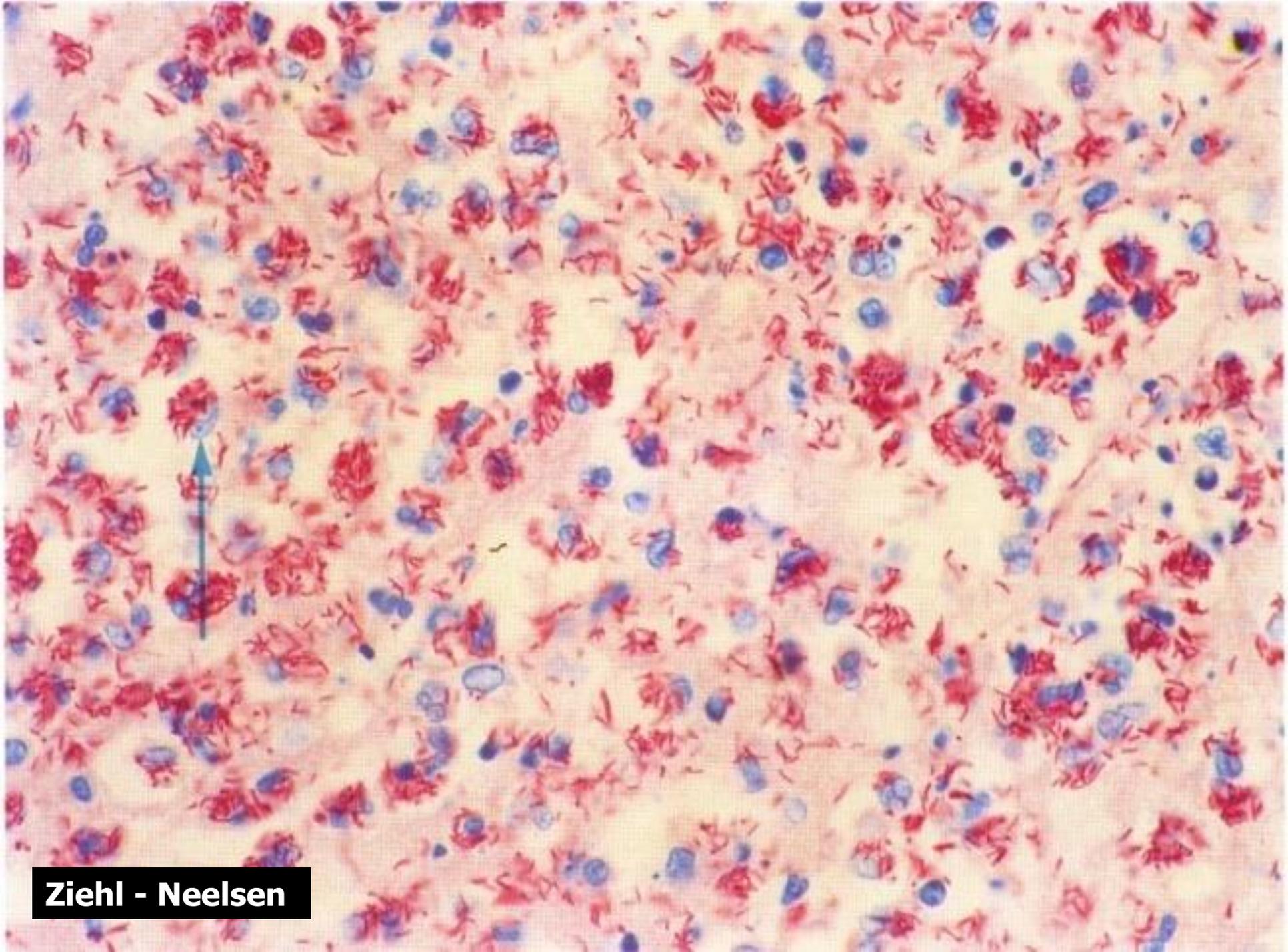


Ghon complex



Caseating granulomata





Ziehl - Neelsen

B-Secondary TB:

Arises in a previously sensitized host in one of following:

- Progressive post primary (shortly after primary).
- Reactivation of old focus.
- Reinfection with a virulent strain.

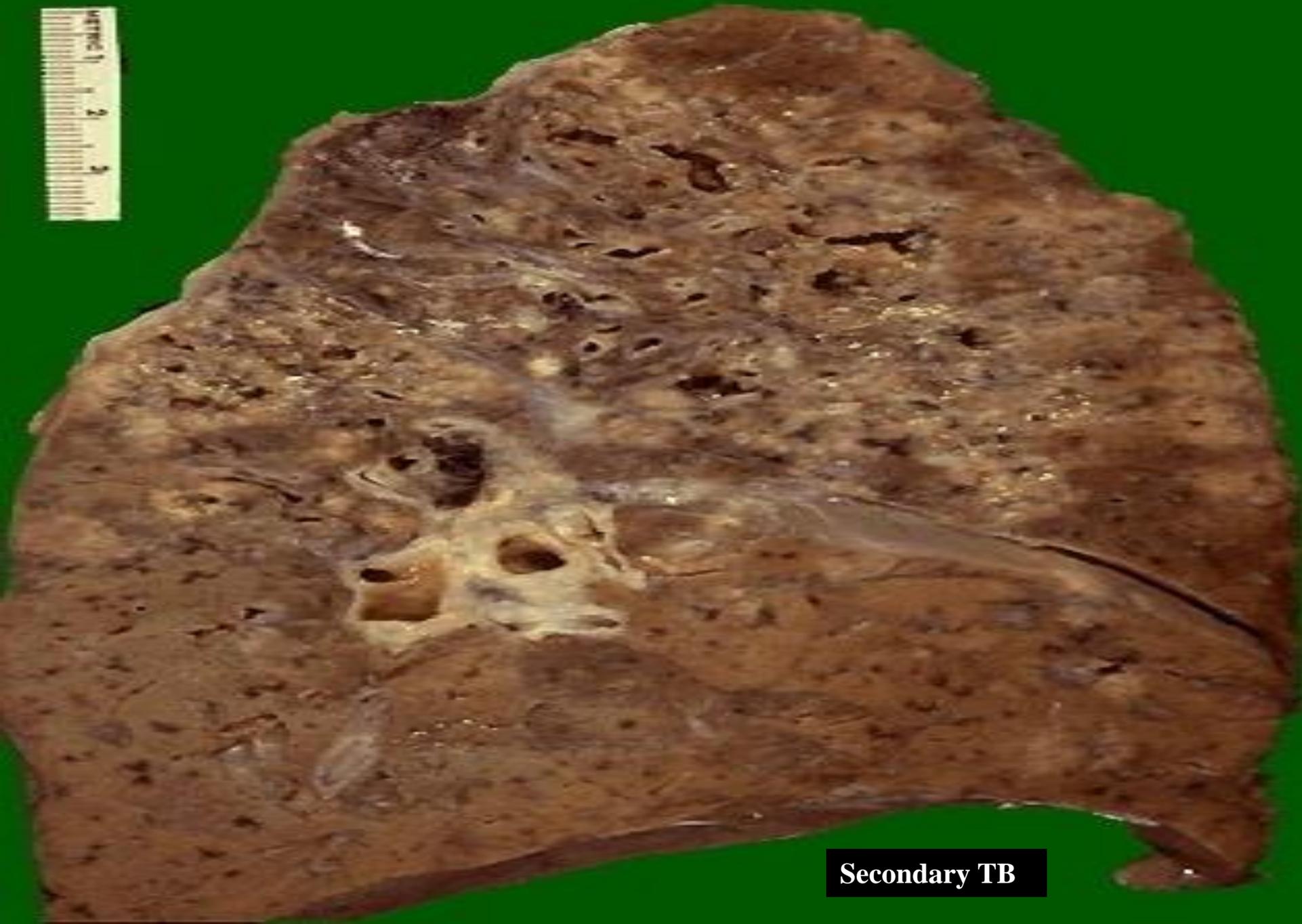
- It is usually localized to apex(of 1 or 2 lobes)(O2).
- Cavitation is common, sputum will be +ve for ZN stain.
- Lymph node enlargement is less prominent (due to wall off).

*Symptoms (any type of TB):

May be asymptomatic or: Hemoptysis ,fever, weight loss and night sweating.

It may heal or become progressive.

*Delayed effect of chronic TB : ***AMYLOIDOSIS***



Secondary TB

Progressive Pulmonary TB

Occurs after primary or secondary TB, along the following routes:

1- Tracheobronchial tree:

- TB-Bronchopneumonia

*larynx → laryngeal TB

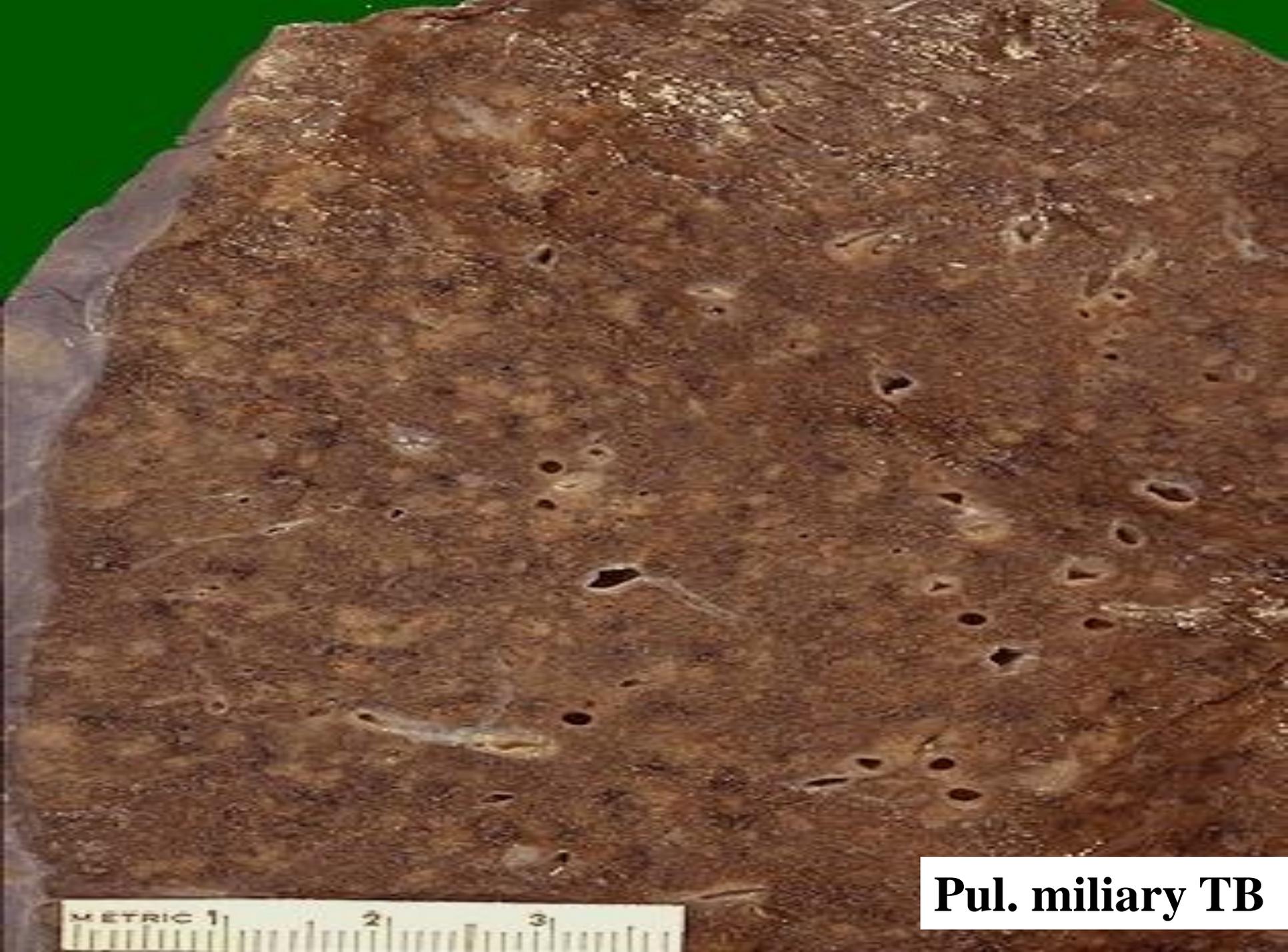
*Pleural involvement leads to effusion, empyema or obliterative fibrous pleuritis.

2-Swallowing infected sputum leads to intestinal TB.

3-Spread through pulmonary veins → Heart → arteries →
→ ***Systemic Miliary TB*** (affects any organ),

4-Through lung lymphatics go to Rt side of hr → and then to lung →
→ ***pulmonary Miliary TB***.

5-Spread through blood → ***Isolated Organ TB*** (Kidney - most common organ to be involved - gives sterile pyurea)



Pul. miliary TB

Tests for Diagnosis of TB

- 1- Sputum** : Direct examination for Acid Fast Bacilli (AFB), Culture of sputum about 6 weeks (best for drug sensitivity).
- 2- Skin test : Tuberculin test** (PPD → positive (48-72hrs.)
- 3-PCR.**

2-Fungal Infections

- Usually infect immunocompromised pt.
- They cause granulomatous reaction \pm . caseation .

- Presentation :

Asymptomatic ,pulmonary infection or systemic disease.

They include Candidiasis, Mucormycosis, *Aspergillosis* ...

Mucormycosis:

Hyphae localized in nose → Lung, brain. Immunocompromised host, especially in diabetics.

Aspergillosis :

- Invasive pulmonary aspergillosis , Aspergilloma (mycetoma) in TB cavity or broncheictasis.
- Allergic bronchopulmonary aspergillosis



Pathology of the Respiratory System-6

DR. ARKAN O. AL-ESAWI
J.B.H , H.S.D.P , M.B CH.B.

LUNG TUMORS

Diagnostic techniques for lung cancer :

1- Chest X ray

2- Sputum Cytology : Simplest noninvasive , should be adequate (alveolar macrophages).

3- Transbronchial biopsy : forceps down into lung parenchyma (by bronchoscope) to take a biopsy.

4- Transcutaneous needle biopsy or FNAC.

5- Open lung biopsy

****Lung tumor are either benign or malignant, and malignant one is either primary or secondary.**

Mainly they are of epithelial origin, but mesenchymal, hematological and germ cells tumors are also encountered.

Lung Hamartoma:

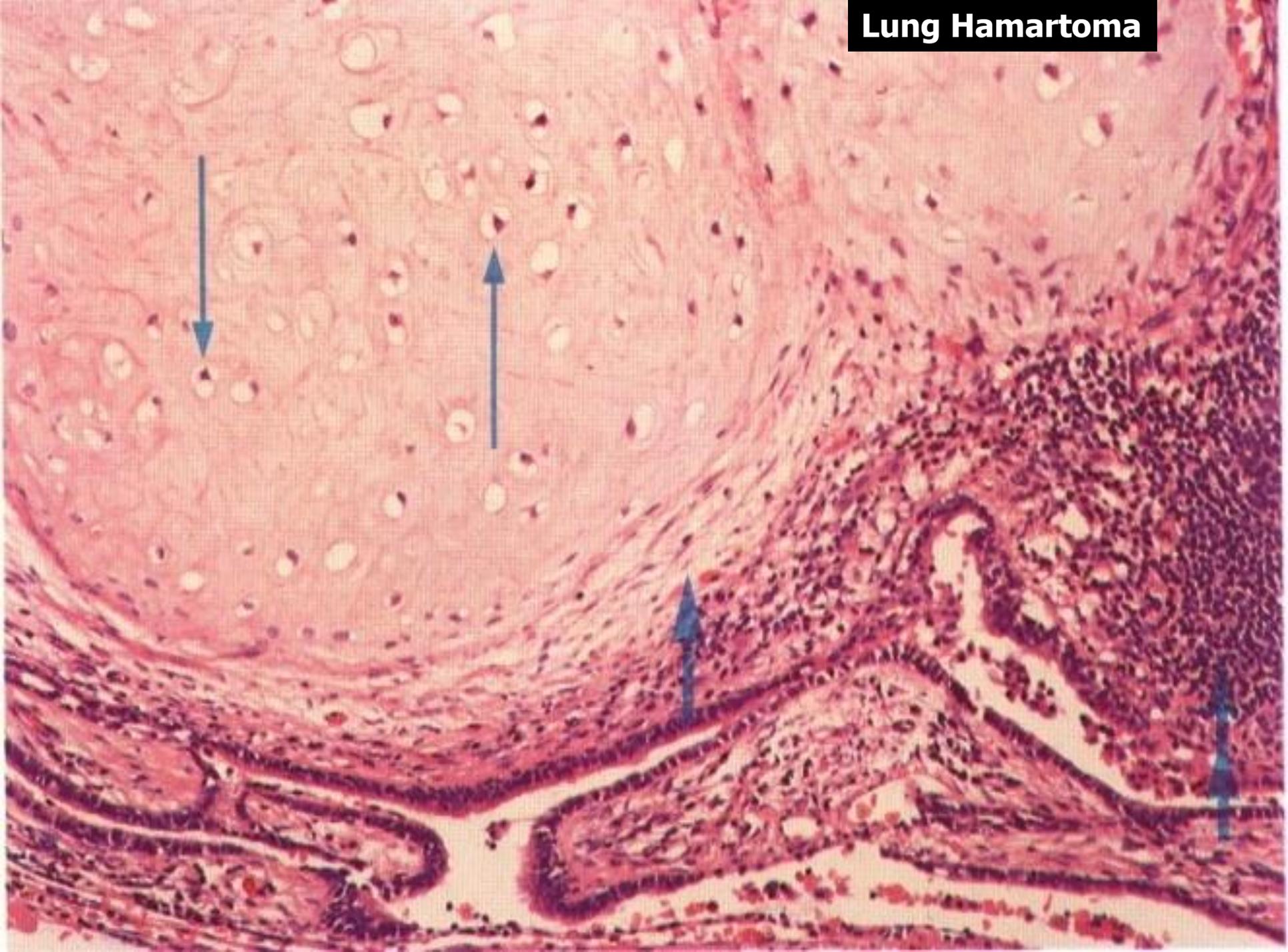
It is a tumor-like lesion consists of cartilage & clefts lined by respiratory epithelium surrounded by connective tissue.

-Incidental.

-Usually peripheral in location(Coin Lesion).

-May simulate tumor radiologically

Lung Hamartoma



MALIGNANT LUNG TUMORS

Primary :

- 95% are bronchogenic carcinoma (SCLC & NSCLC).

- REMAINING 5% Includes :

Bronchial carcinoids, Bronchial gland tumors, Mesenchymal tumors (sarcoma), Lymphomas....

Secondary : Commoner than primary tumors.

Etiology:

1- Cigarette smoking :

up to 90% of patients are smokers especially squamous & small cell CA.

The **risk** in average and heavy smokers is **10** times and **60** times greater than non-smoker respectively.

- Passive smoking (proximity to smokers) ↑ risk twice that of nonsmokers

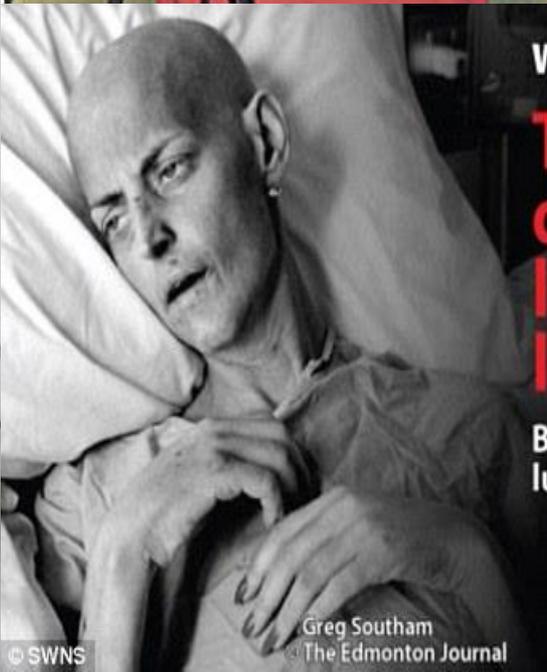
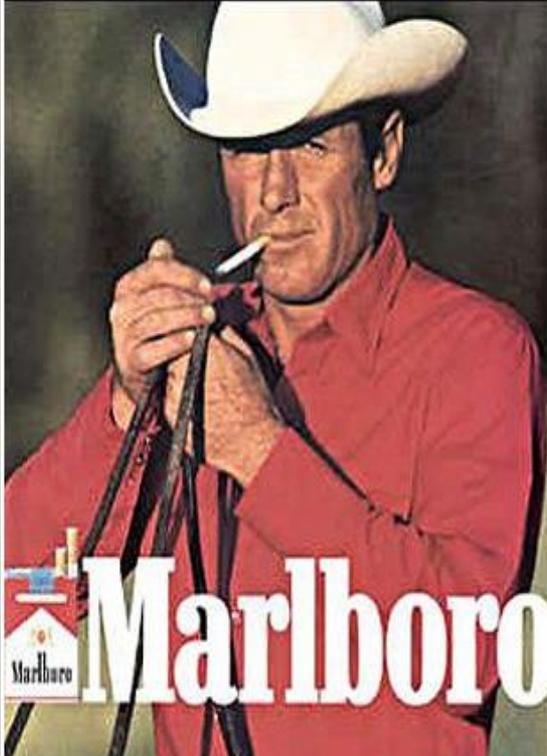
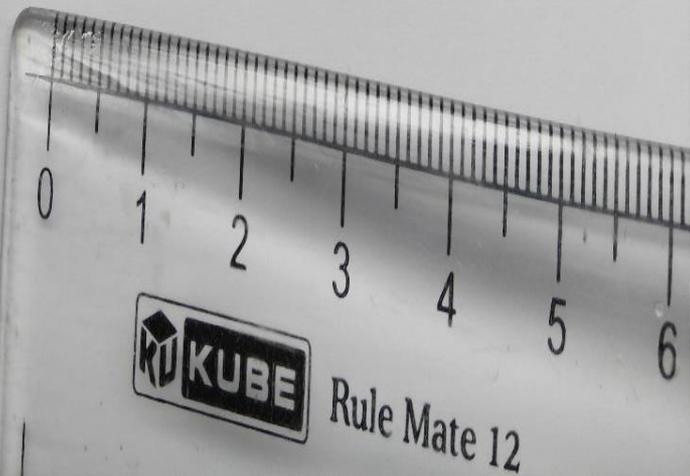
2-Asbestos:

Asbestos alone increases the risk of ca-lung 5 times but in combination with smoking it increases the risk 50- (...90) times. (smoking alone /mesothelioma).

- Others: uranium, nickel , arsenic , chromate , radiation.....

3- Scarring in lung tissue (Scar Cancer).

4-Genetic defect .



WARNING

**This is what
dying of
lung cancer
looks like.**

Barb Tarbox died at 42 of
lung cancer caused by smoking.

You can quit. We can help.
1-888-888-8888
internet/url.ca

Appearance of bronchogenic carcinoma:

- Central or peripheral.
- CA in situ → thick mucosa.....infiltration of bronchial wall into lung parenchyma.
- Hemorrhage, ulceration & necrosis may be seen

Microscopic variants include :

1-Nonsmall Cell Carcinoma ~(80-85%):

- squamous cell ca.
- adenocarcinoma
- large cell ca.

2-Small Cell Carcinoma ~(15%).

3-Others.

A-NON SMALL CELL CARCINOMA

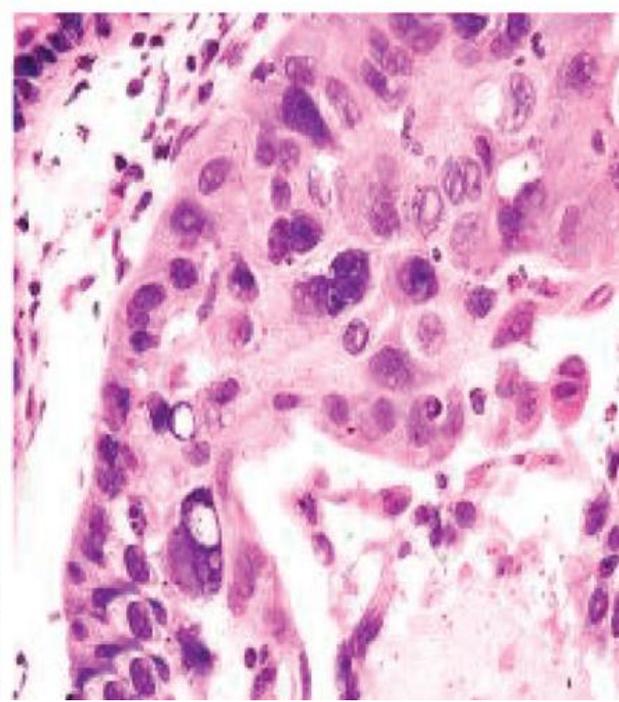
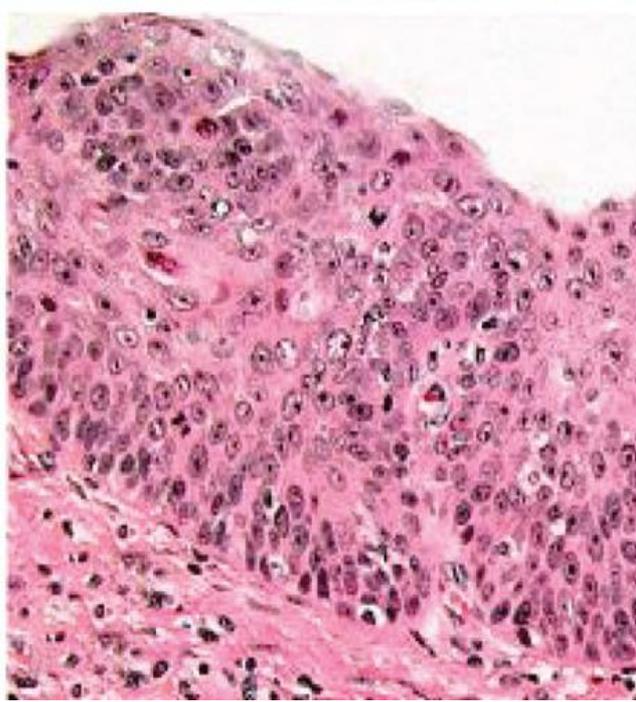
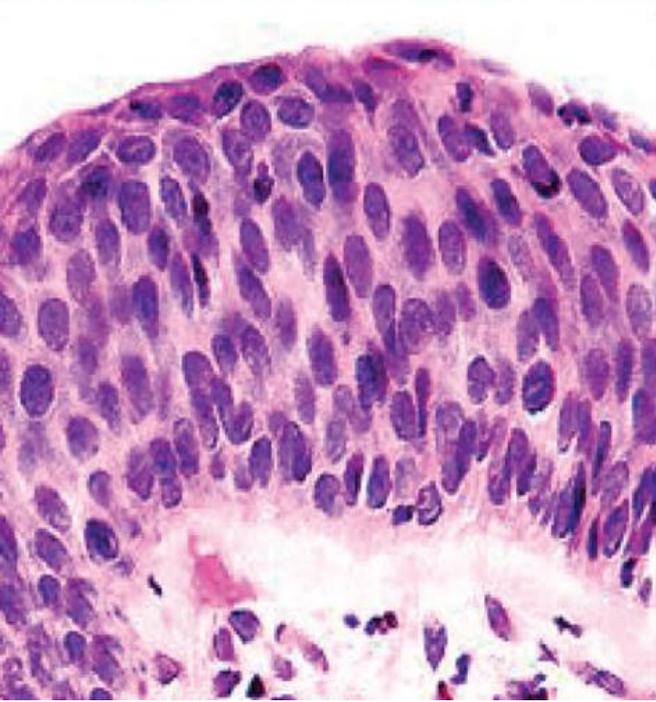
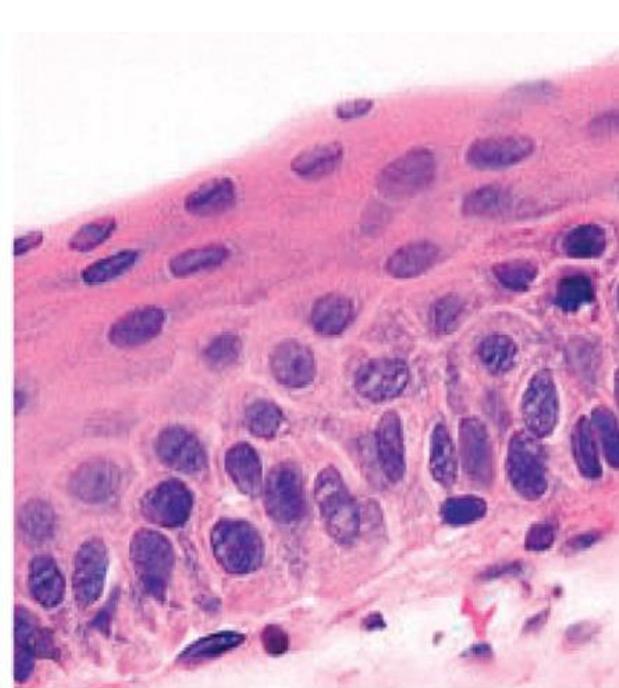
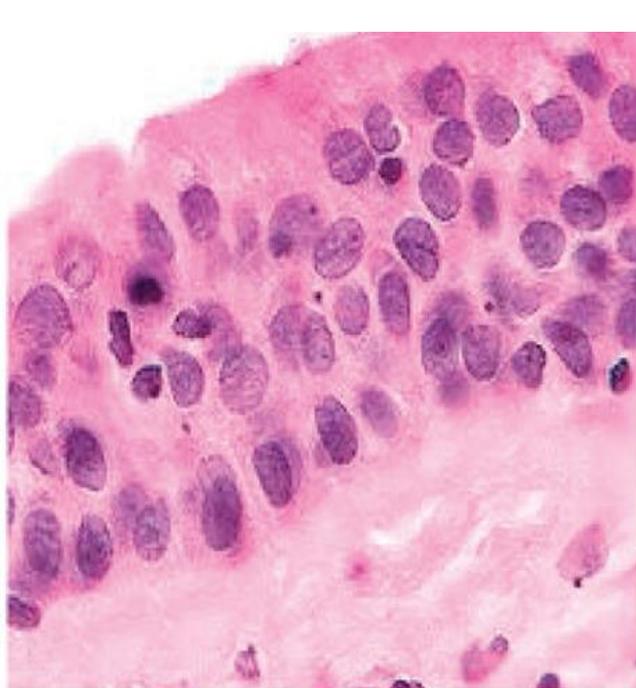
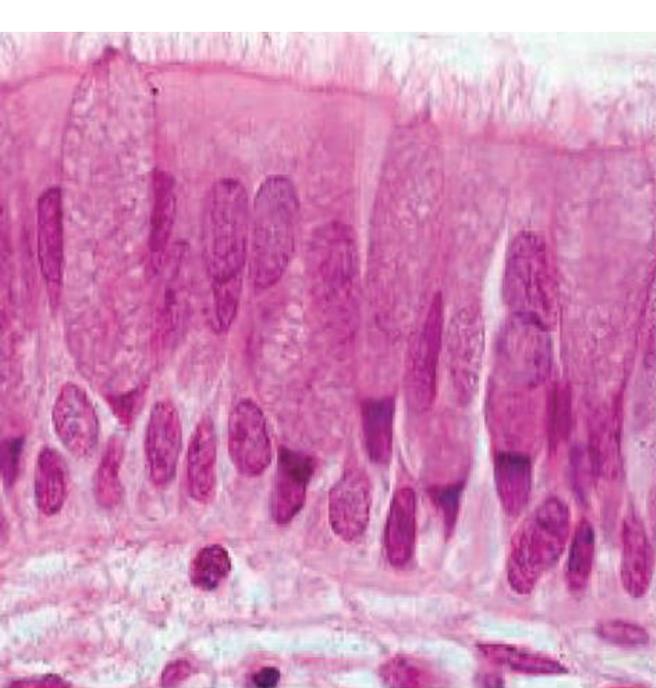
1- Squamous cell carcinoma :

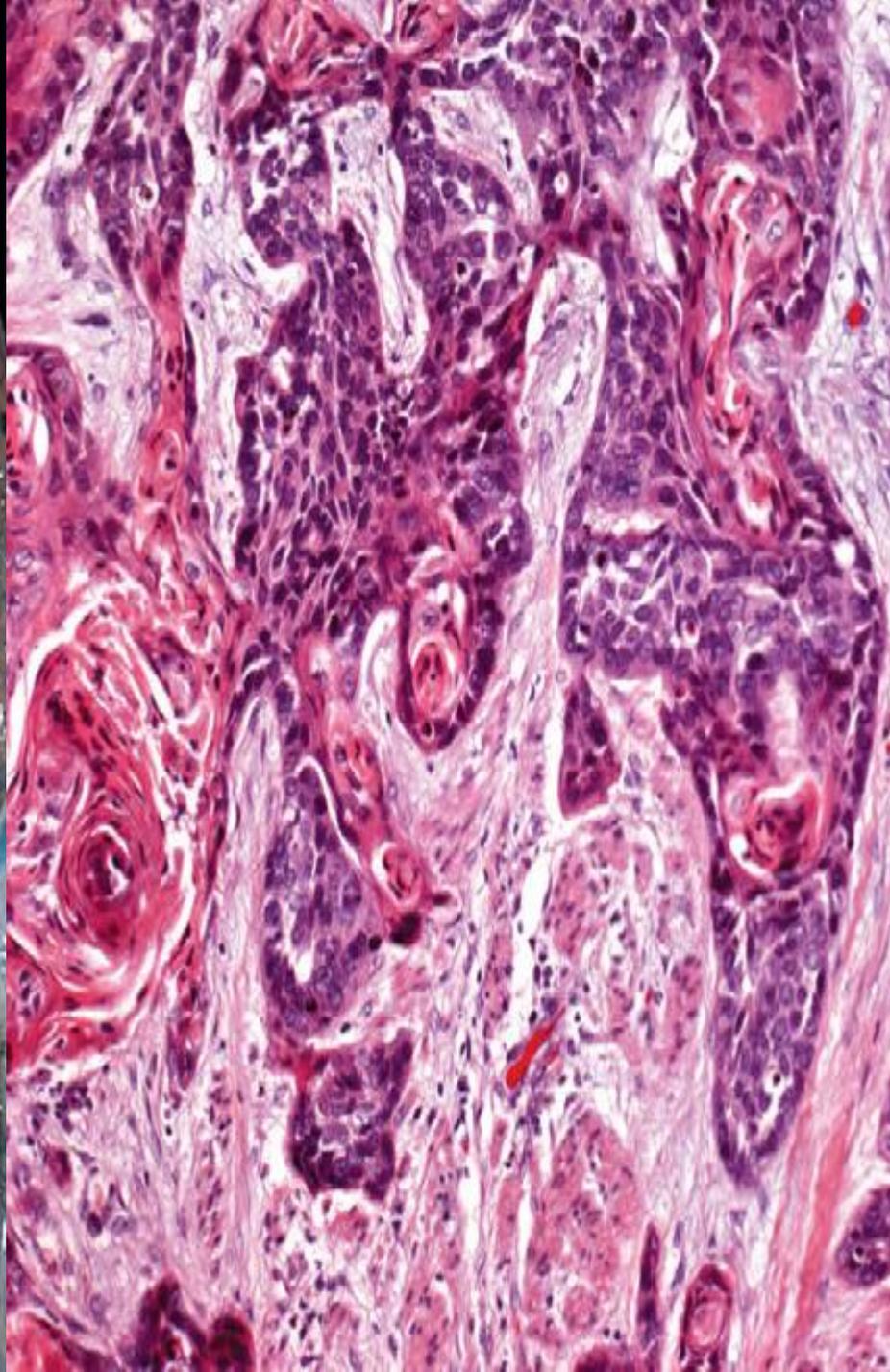
- ~ 30% of NSCLC ,
- Male > female,
- > 90% associated with smoking
- Majority are hilar (central)
- Spread to local , then regional lymph nodes
- Metastases later than small cell.

Histology :

Well differentiated (keratinization) or undifferentiated

- Hypercalcemia more common than other types (PTH-related peptides “paraneoplastic syndrome”) or bone metastasis.





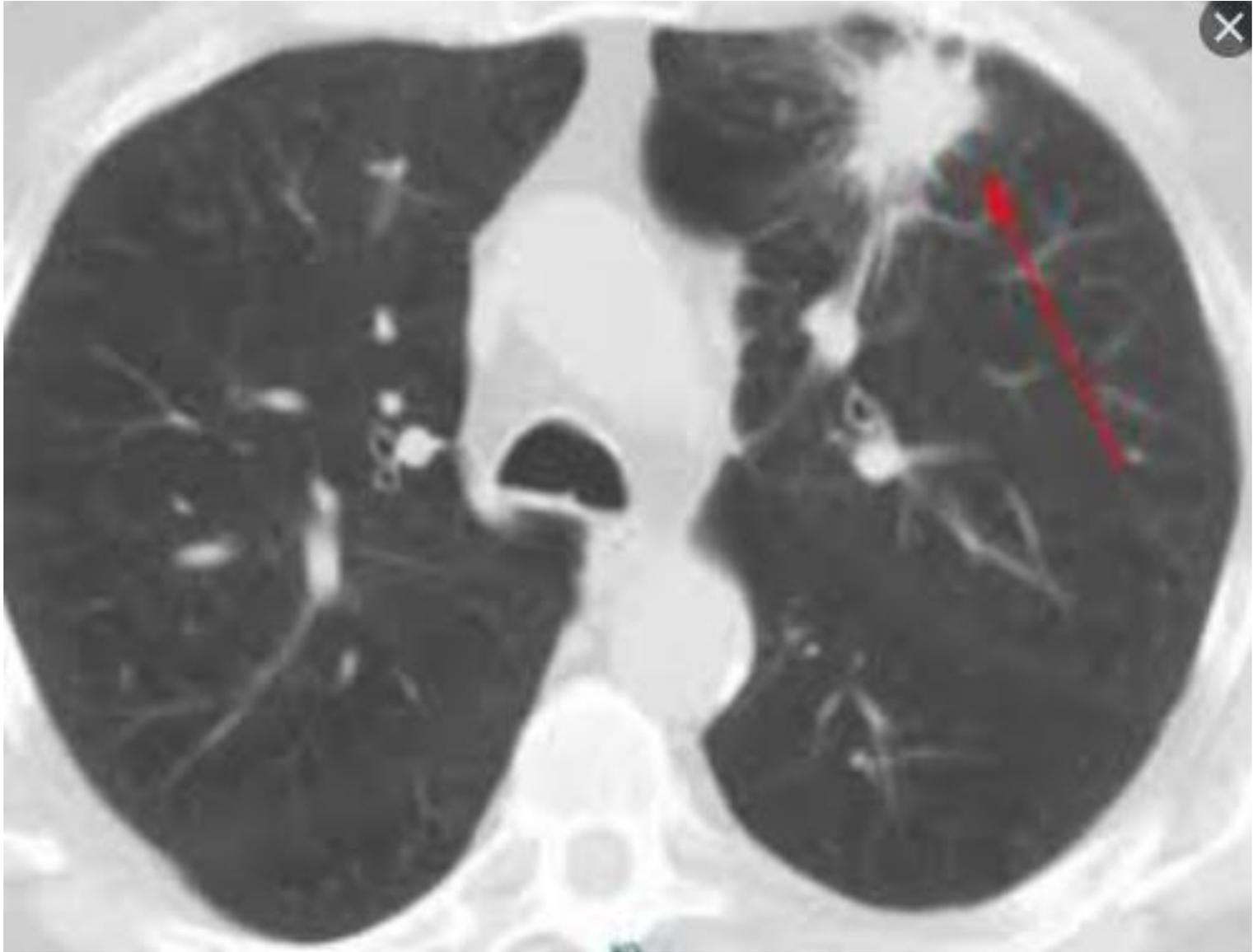
2- Adenocarcinoma ~ 40% of NSCLC

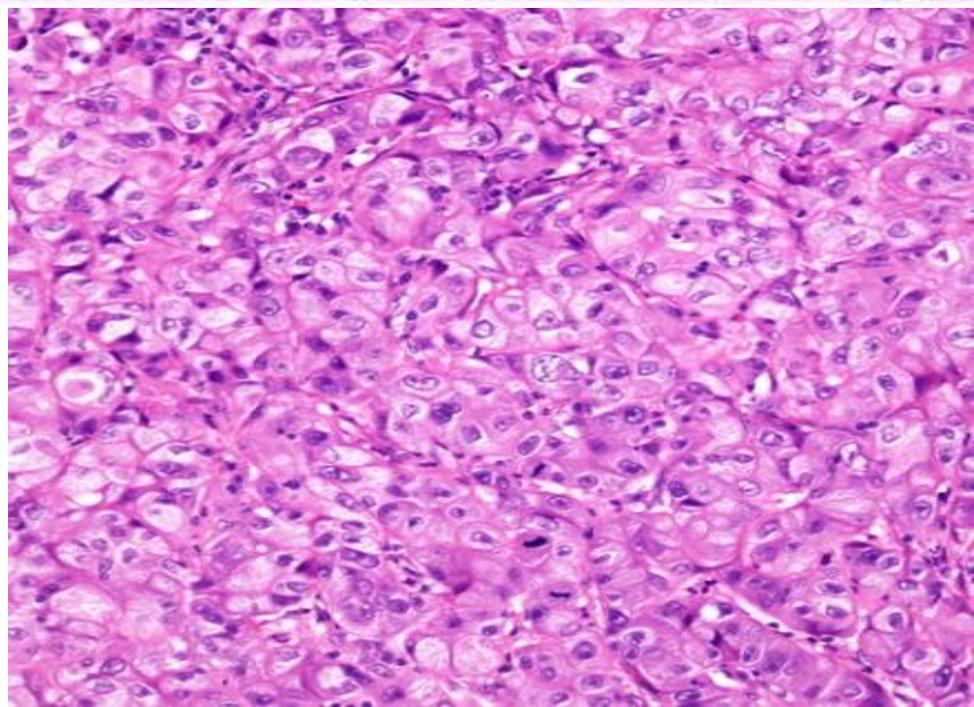
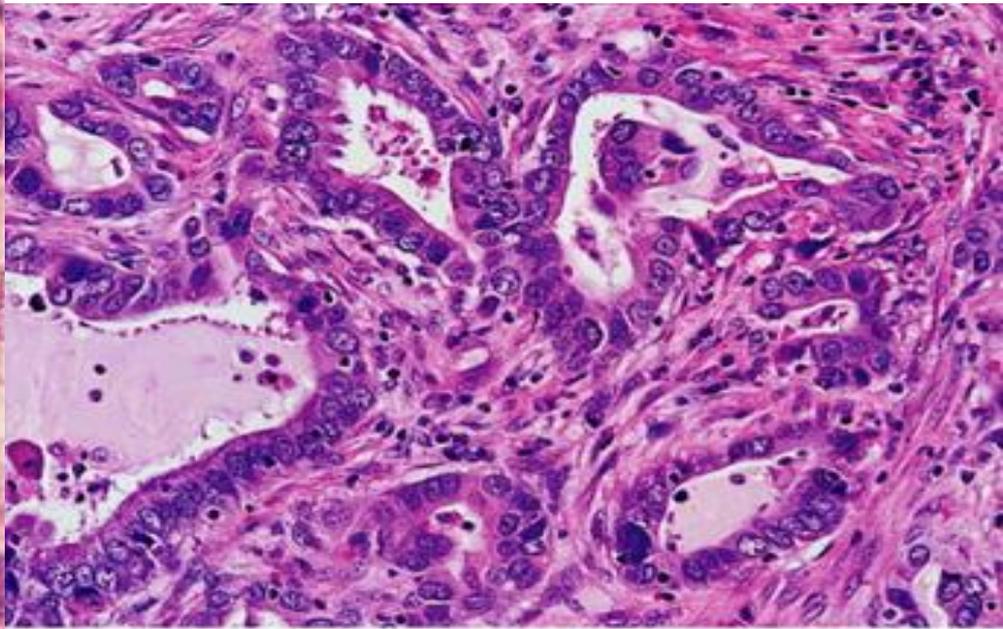
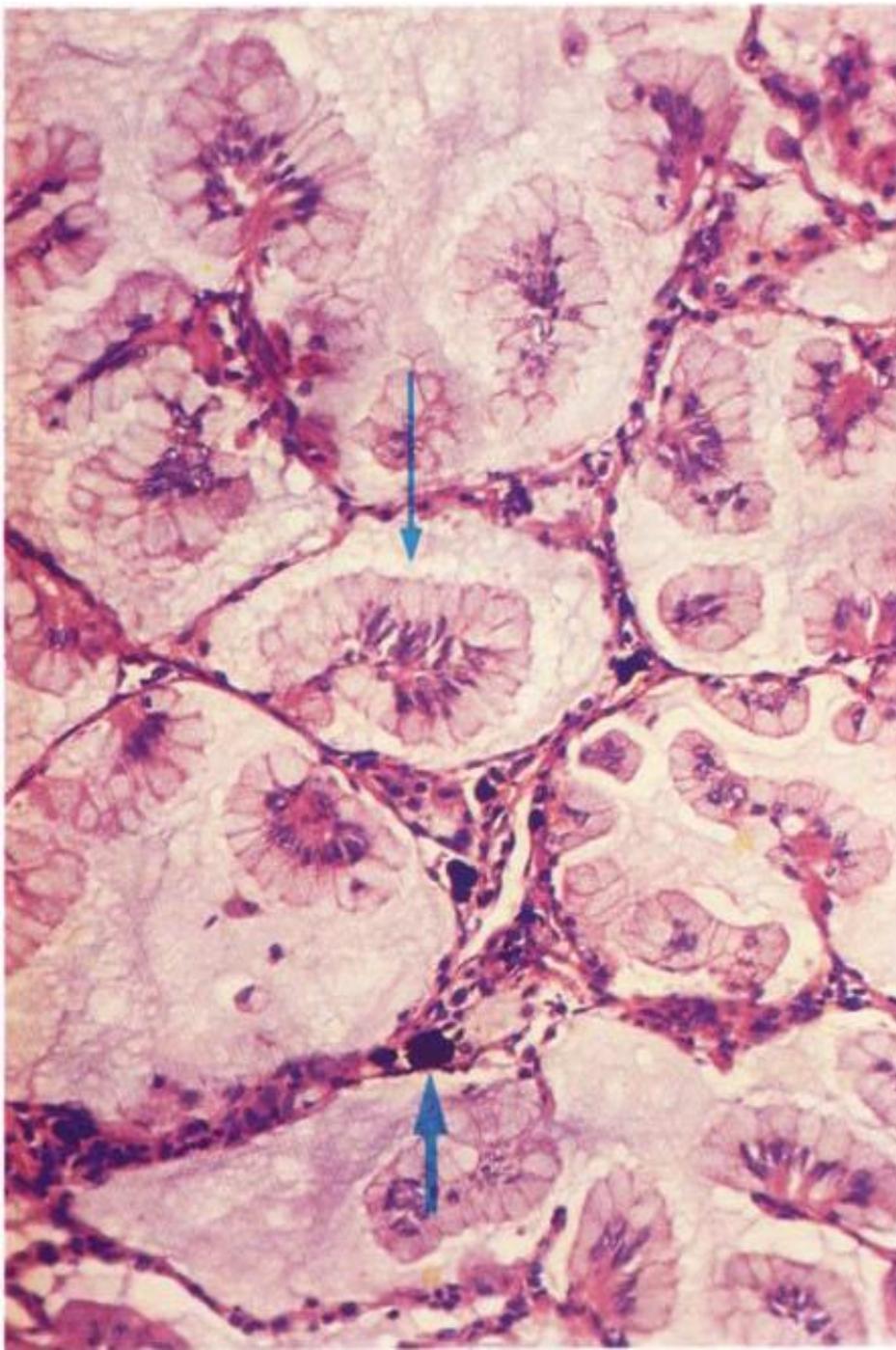
- Male = Female (but it is the most common type in female and non smoker).
- Least associated with smoking.
- Usually peripheral rather than central.
- Growth is slower than squamous but with early metastasis.

- Histological types :

Acinar (gland-forming), solid, papillary, mucinous

- **Adenocarcinoma in situ (AIS), formerly called bronchioloalveolar carcinoma** : multifocal, diffuse or localized nodule(s) of columnar cells that grow along preexisting bronchioles and alveoli; without destructive pattern, peripheral in location and may present as pneumonic consolidation.





3- Large cell (anaplastic) carcinoma :

- Poorly differentiated tumors
- Difficult to type, may need special immunostains.
- About 10 %.
- Prognosis is poor
- It includes :
 - * Poorly differentiated Squamous Cell CA.
 - * Poorly differentiated Adenocarcinoma.
 - * Clear Cell .
 - * Anaplastic carcinoma.

B-SMALL CELL CARCINOMA

- Incidence ~ 15% , Male > Female.
- Over 90% is associated with smoking.
- Arises from neuroendocrine cells.
- Usually hilar (Central).
- Most aggressive ,frequent necrosis, metastasize early.
- Most frequent type in regarding to ectopic hormones
- (ADH , ACTH , Carcinoid Syndrome ...etc)**

-Histology : -

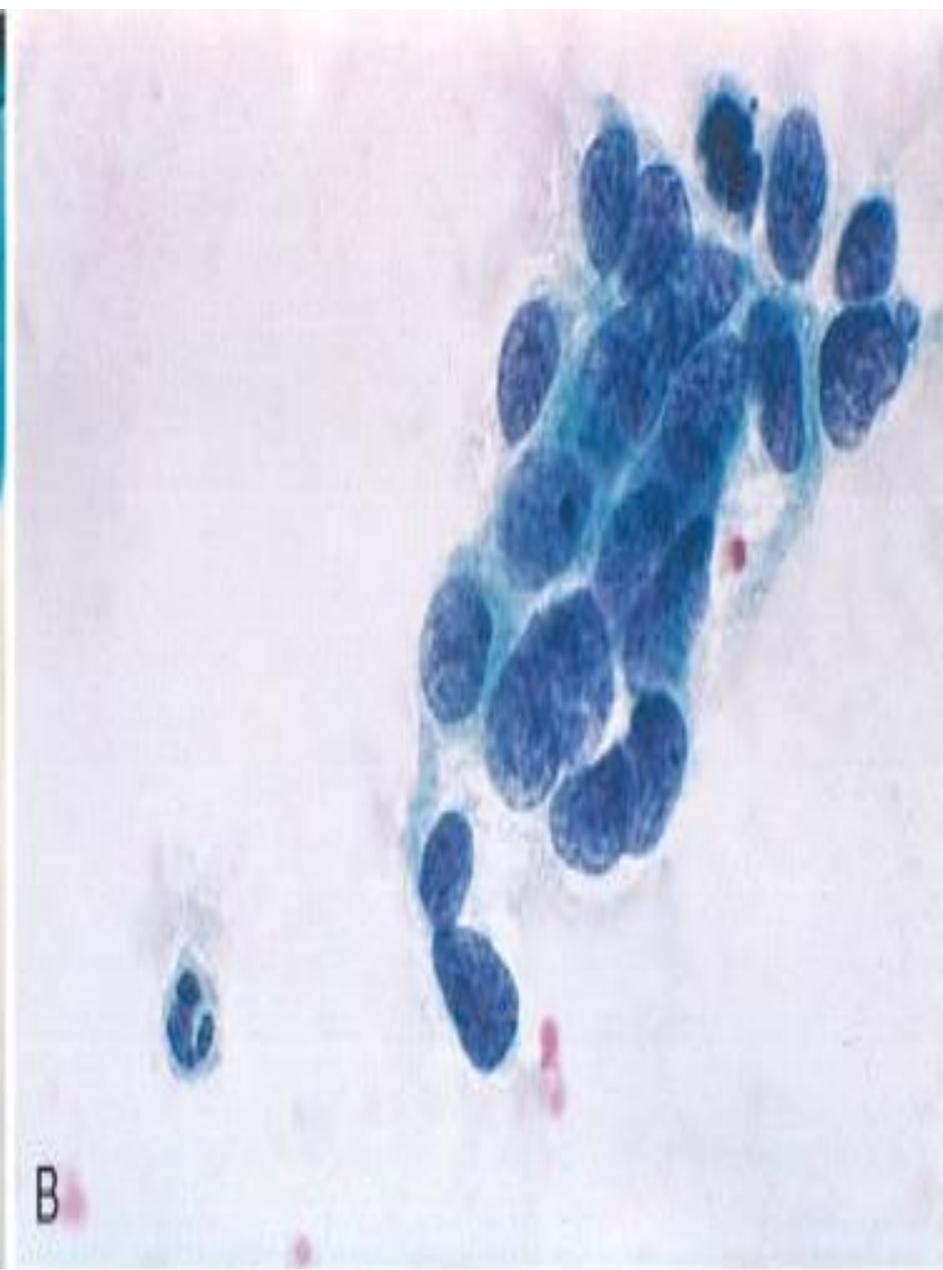
-Small round blue cells , no obvious nucleoli , frequent mitosis with necrosis..

****Combined patterns are also present(SCLC & NSCLC)**



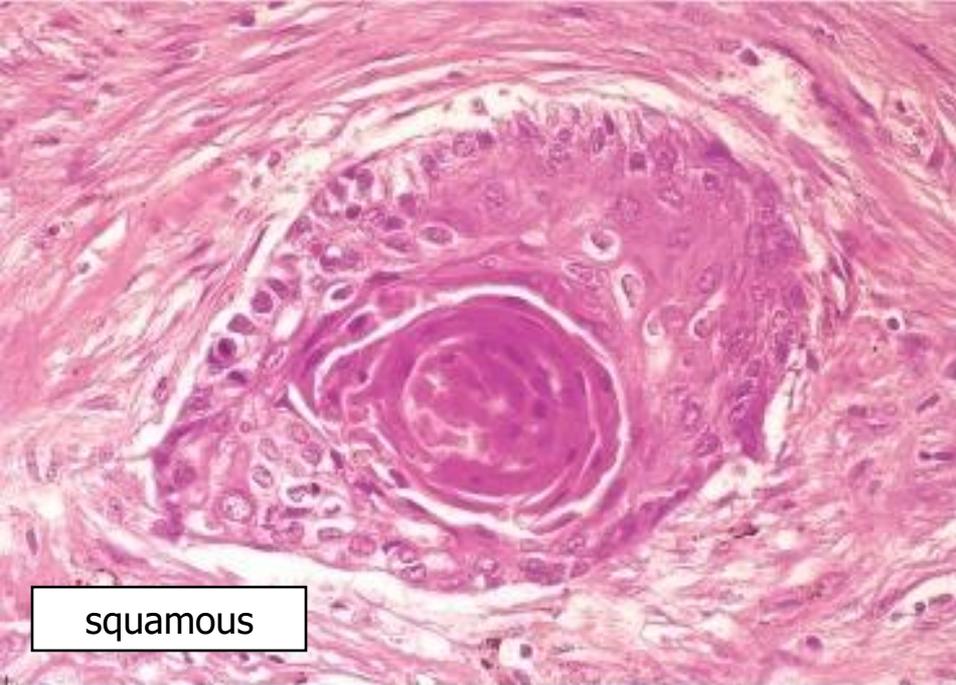
A

A- Squamous cell CA

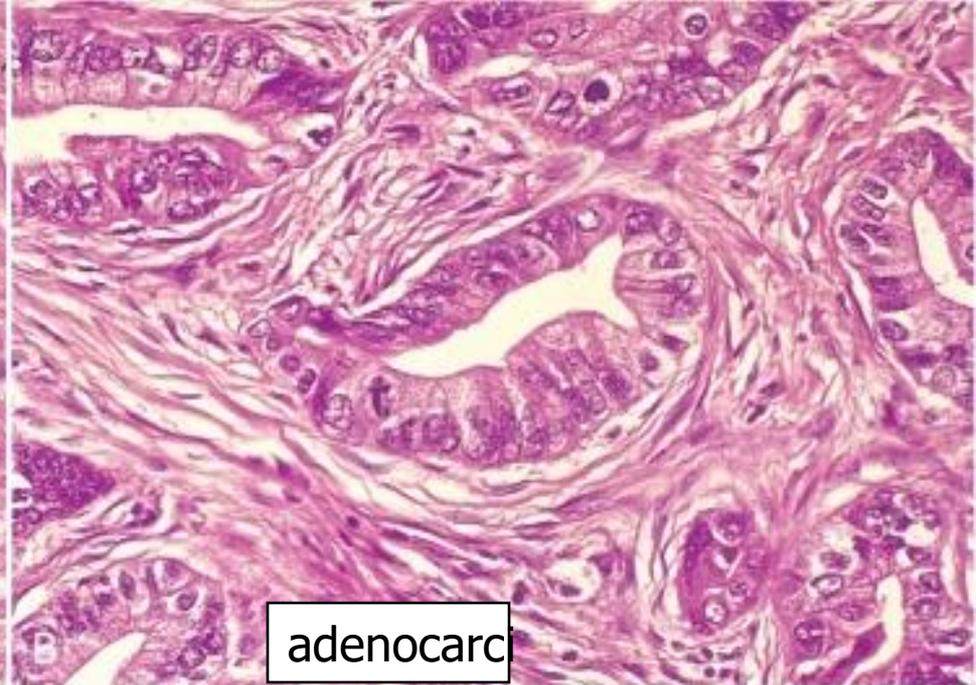


B

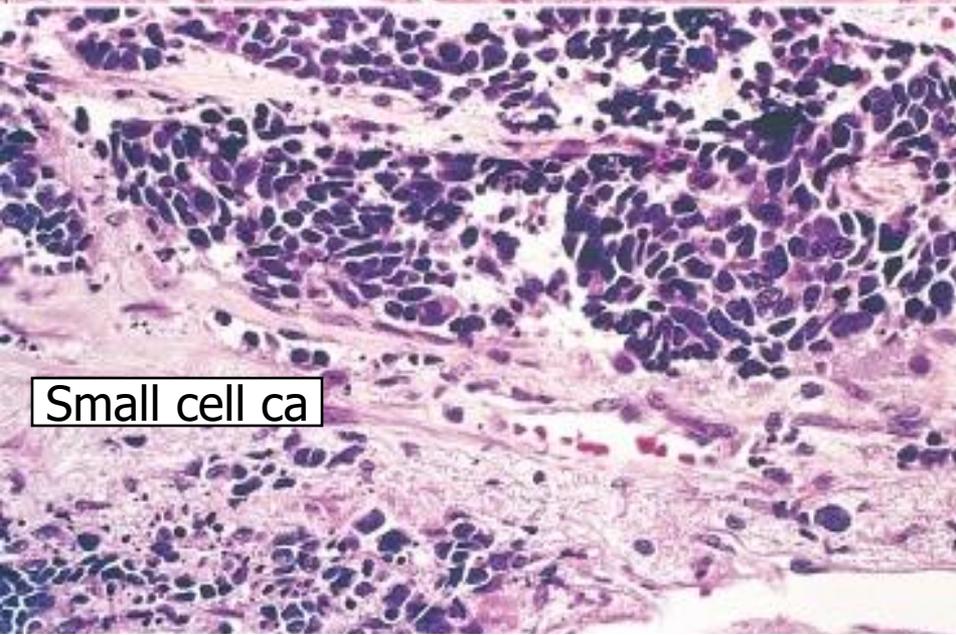
B- Small Cell CA



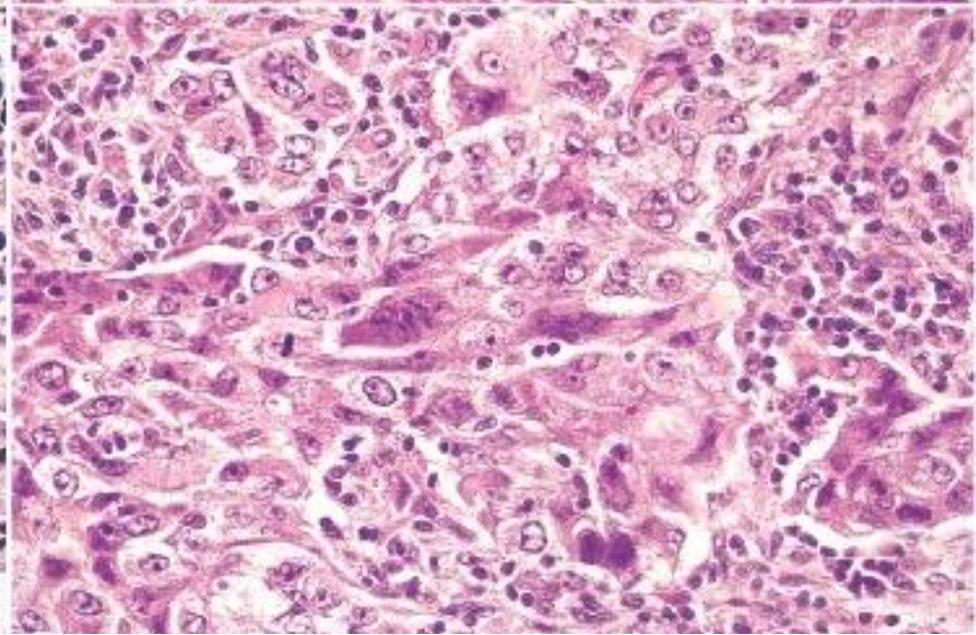
squamous



adenocarc



Small cell ca



Types of Bronchial Carcinoma

Spread of lung cancer :

- 1- Local extension: Pleura , pericardium ,mediastinum...
- 2- Lymph node metastases.
- 3- Distant metastases :Adrenal ? ,Liver

Local & secondary effects of lung cancer:

1-Local & regional effects :

Central :

e.g. cough, hemoptysis, obstruction, atelectasis, pneumonia, abscess

Peripheral: e.g. incidental, hemoptysis or pneumonia.

Local & regional invasion :

e.g. *Mediastinal invasion*, recurrent laryngeal n. on left side →vocal cord Paralysis.

2- **Extra-thoracic Metastases:** eg. bone → # & ↑Ca⁺⁺.

3- Paraneoplastic Syndrome :

Presents in 5-10% of lung tumors, mostly in small cell CA.

Includes:

- Ectopic hormone production :

* ADH , ACTH, Calcitonin ,Cushing synd ...

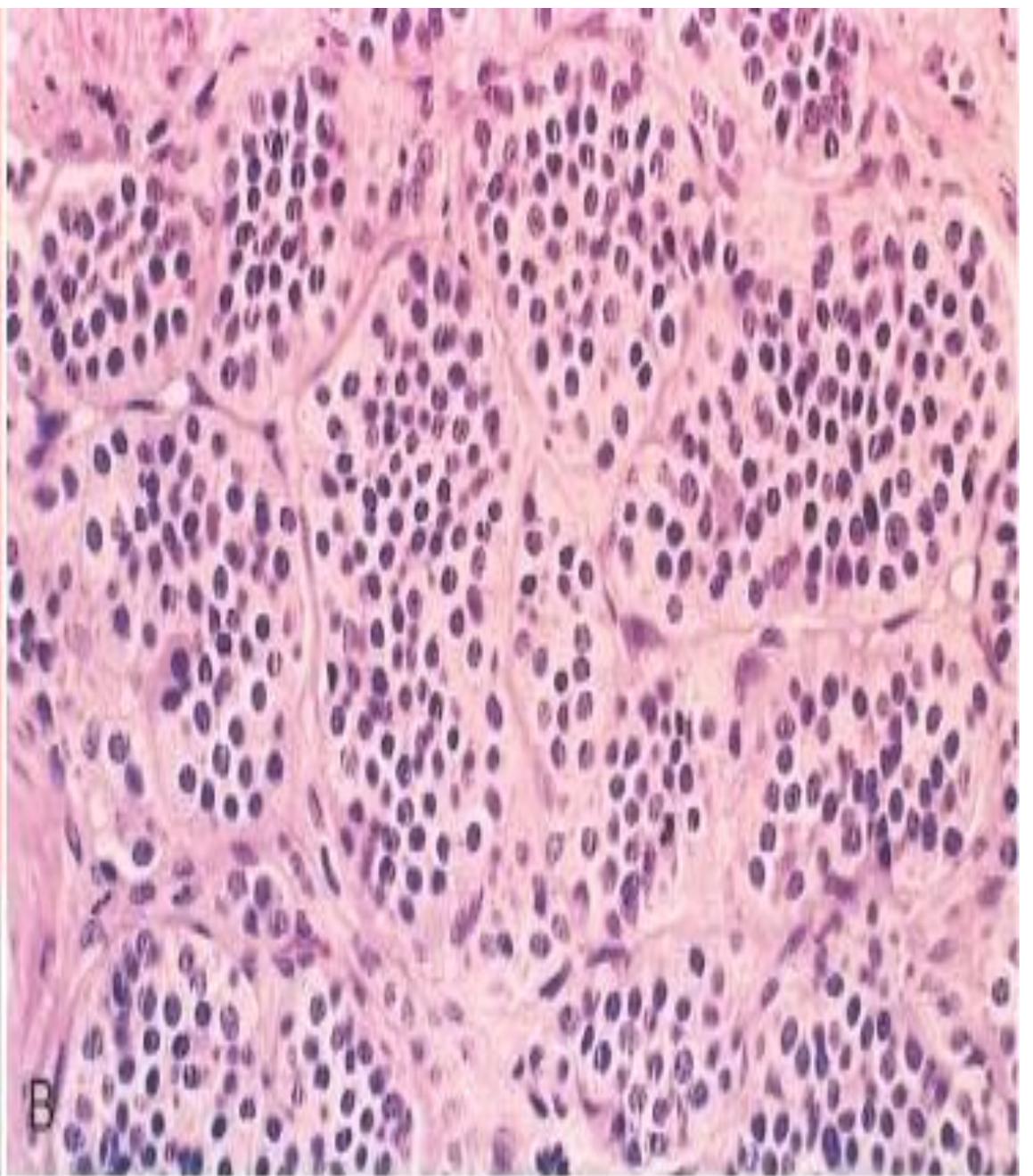
*PTH like hormone in squamous cell ca(hyper- calcemia).

-Digital clubbing & hypertrophic osteoarthropathy.

-Neuromuscular disorders (~myasthenic syndrome)

Carcinoid Tumor (neuroendocrine Tumor, Grade I)

- Younger age than CA , (~ 5%) of lung tumors
- Arises from neuroendocrine cells
- Intraluminal growth (polypoid), infiltrates wall
- Histology :
 - * **Uniform cells , absent mitoses , arranged in nests & cords**
 - * **Few show mitoses , necrosis, atypia (*Atypical Carcinoid*)**
- Symptoms of obstruction & infection
- May secrete serotonin (Carcinoid syndrome)
- Surgery is curative in most cases .
- Atypical carcinoid (atypia , mitosis , necrosis) ..is more aggressive.



Carcinoid tumor

Metastatic tumors in lung

- More common than primary.
- Most types of carcinomas & sarcomas can metastasize to the lung.
- Reach the lung by lymphatic or by hematogenous route.
- Grossly may show :
 - multiple nodules , (Cannon Ball)
 - single nodule
- Pleural effusion is common in metastatic tumors.



Pathology of the Pleura

- **Pleural Effusion**
 - * Transudate - Heart failure
 - * Exudate - Pneumonia
 - * Hemorrhagic - Cancer , Tuberculosis
- **Hemothorax**: trauma , rupture aneurysm
- **Pyothorax** : turbid effusion with numerous polymorphs neutrophils, usually complicating bacterial pneumonia.
- **Empyema**: variant of pyothorax, with thick pus in the pleural cavity, often followed by fibrosis.
- **Chylothorax** : accumulation of milky, lipid rich fluid due to lymphatic obstruction, usually by tumor

Mesothelioma :

- Rare malignant tumors of mesothelial cells with poor prognosis can affect the pleura , peritoneum, pericardium & tunica vaginalis.
- up to 90% are ASBESTOS-related
- **Grossly**: A diffuse lesion surrounding& infiltrating lung.

- **Microscopically**:
- **Mixture of spindle cells (Sarcoma like) and glandular elements (Adenocarcinoma)**

