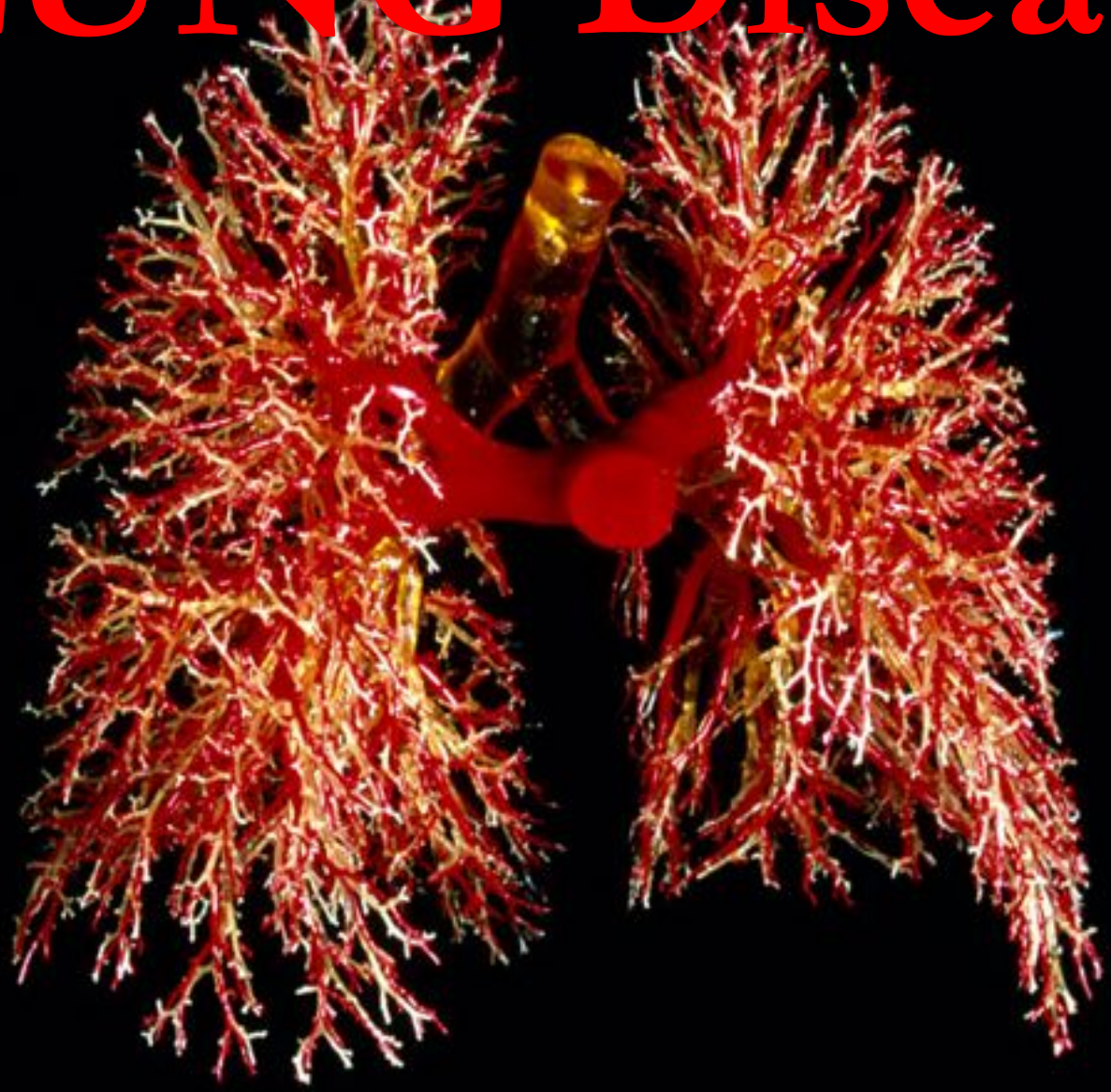
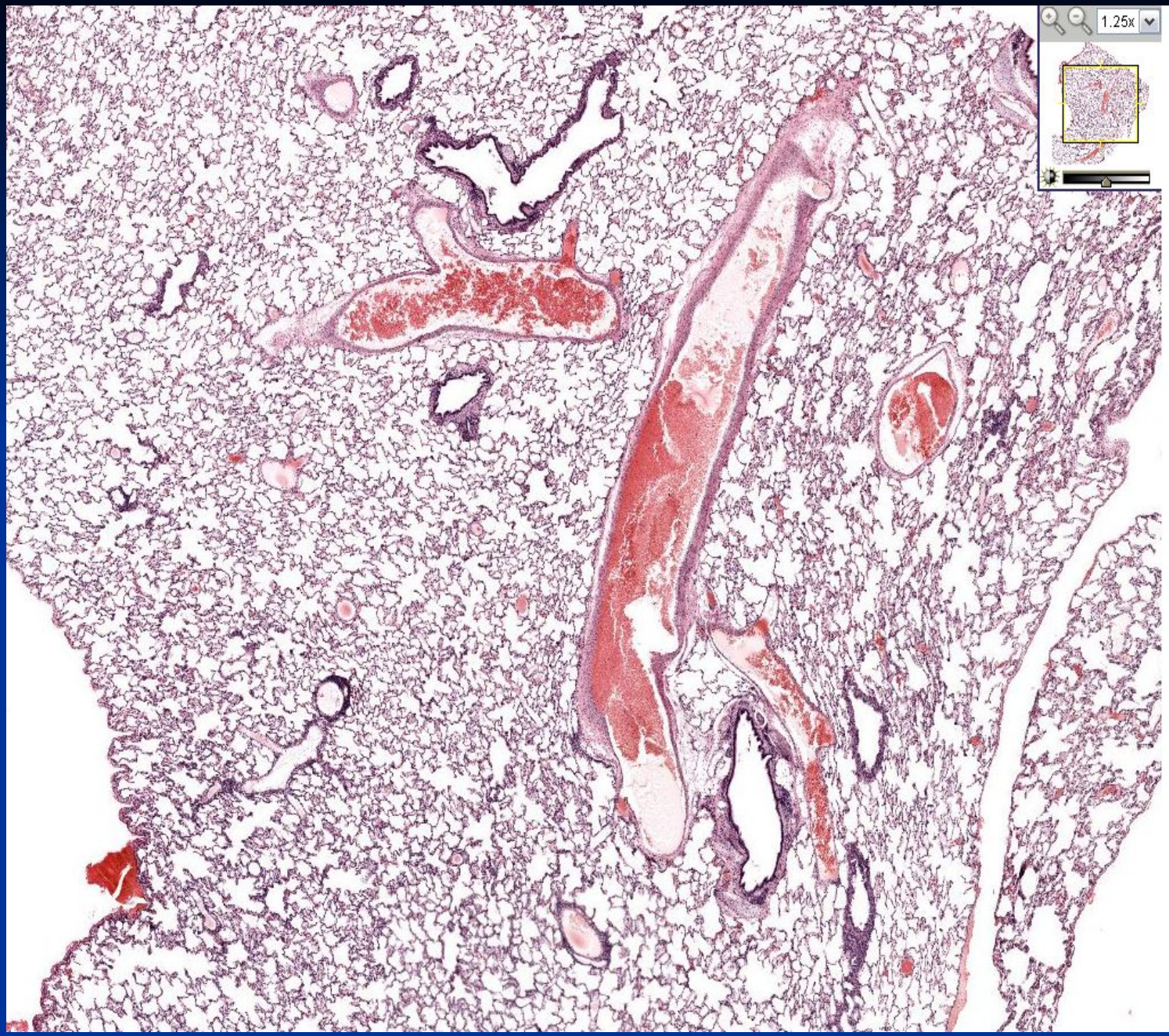
LUNG Diseases

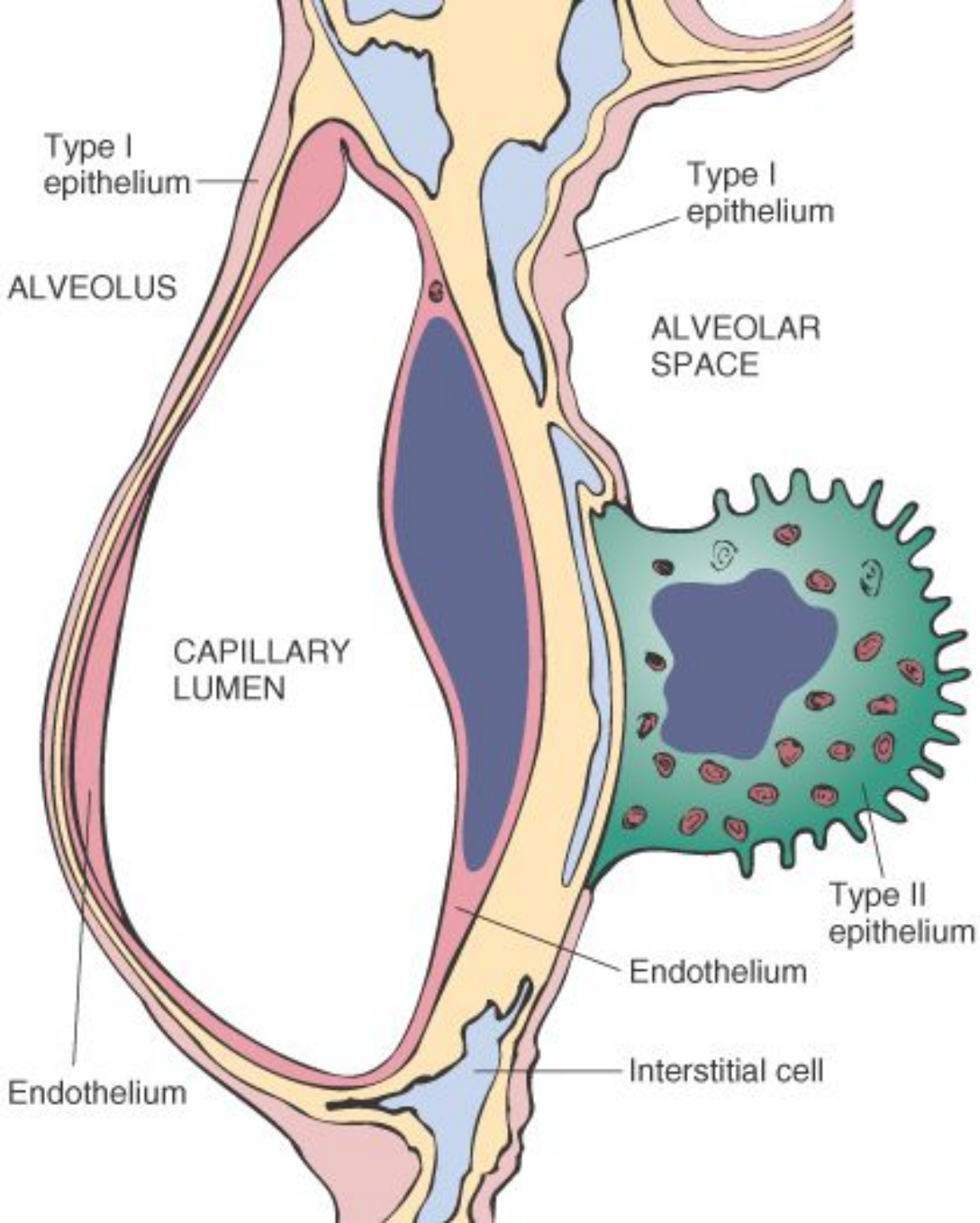


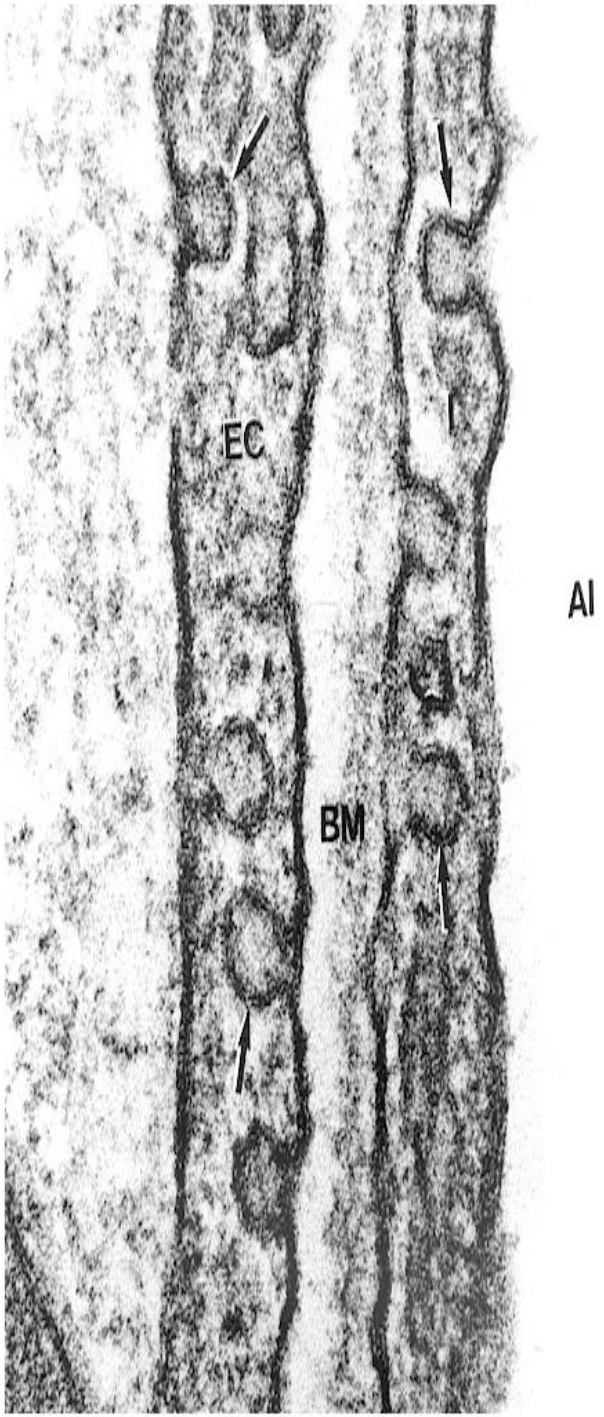
Function of the Respiratory System

- Oversees gas exchanges (oxygen and carbon dioxide) between the blood and external environment
- Exchange of gasses takes place within the lungs in the alveoli(only site of gas exchange, other structures passageways
- Passageways to the lungs purify, warm, and humidify the incoming air
- Shares responsibility with cardiovascular system

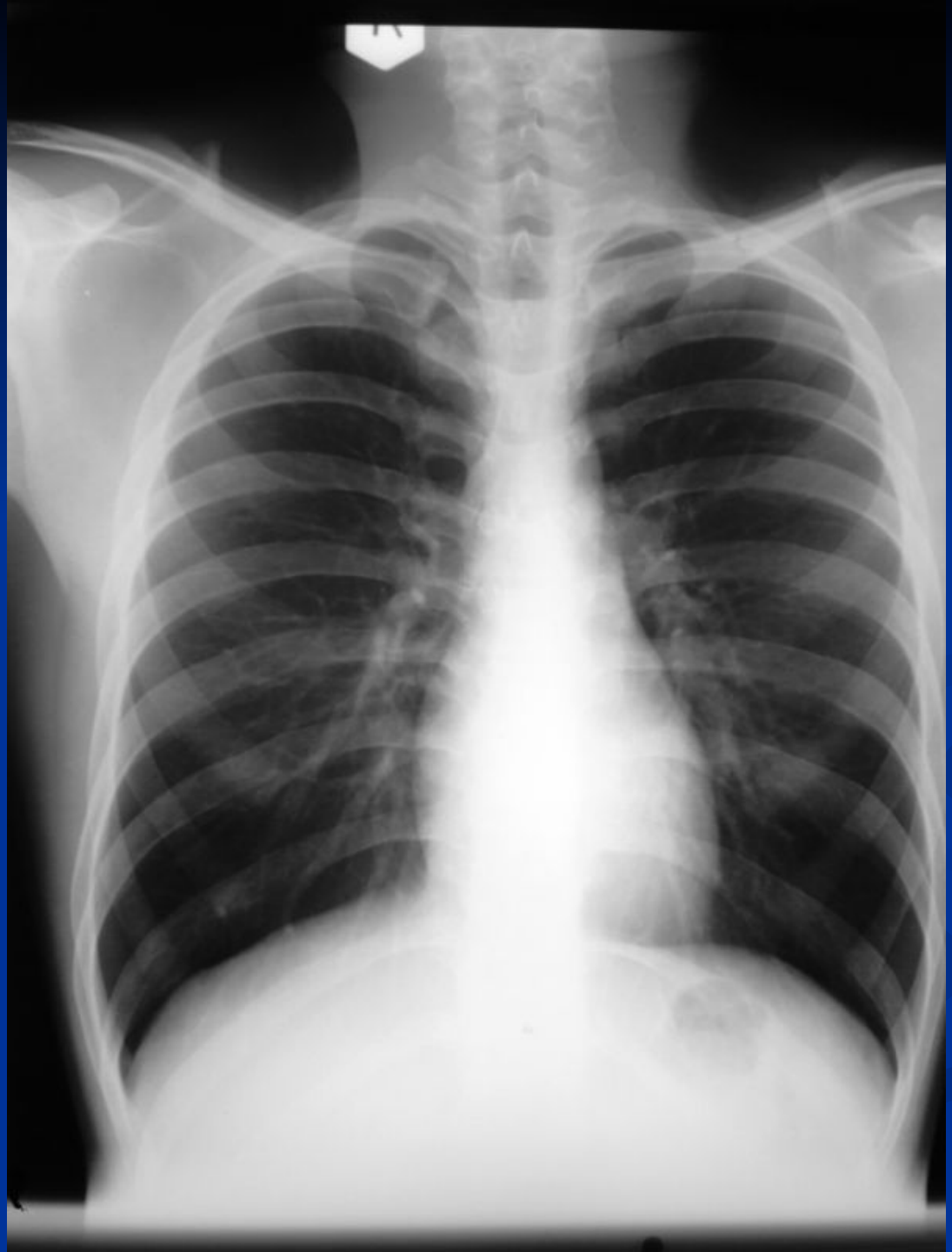


- Bronchi
- Bronchioles
- Terminal bronchioles
- Alveolar ducts
- Alveoli
- Type 1 pneumocytes
- Type 2 pneumocytes
- Macrophages
- Capillaries


Type I epithelium
Type I epithelium
ALVEOLUS
ALVEOLAR SPACE
CAPILLARY LUMEN
Type II epithelium
Endothelium
Interstitial cell
Endothelium


EC
BM
Al

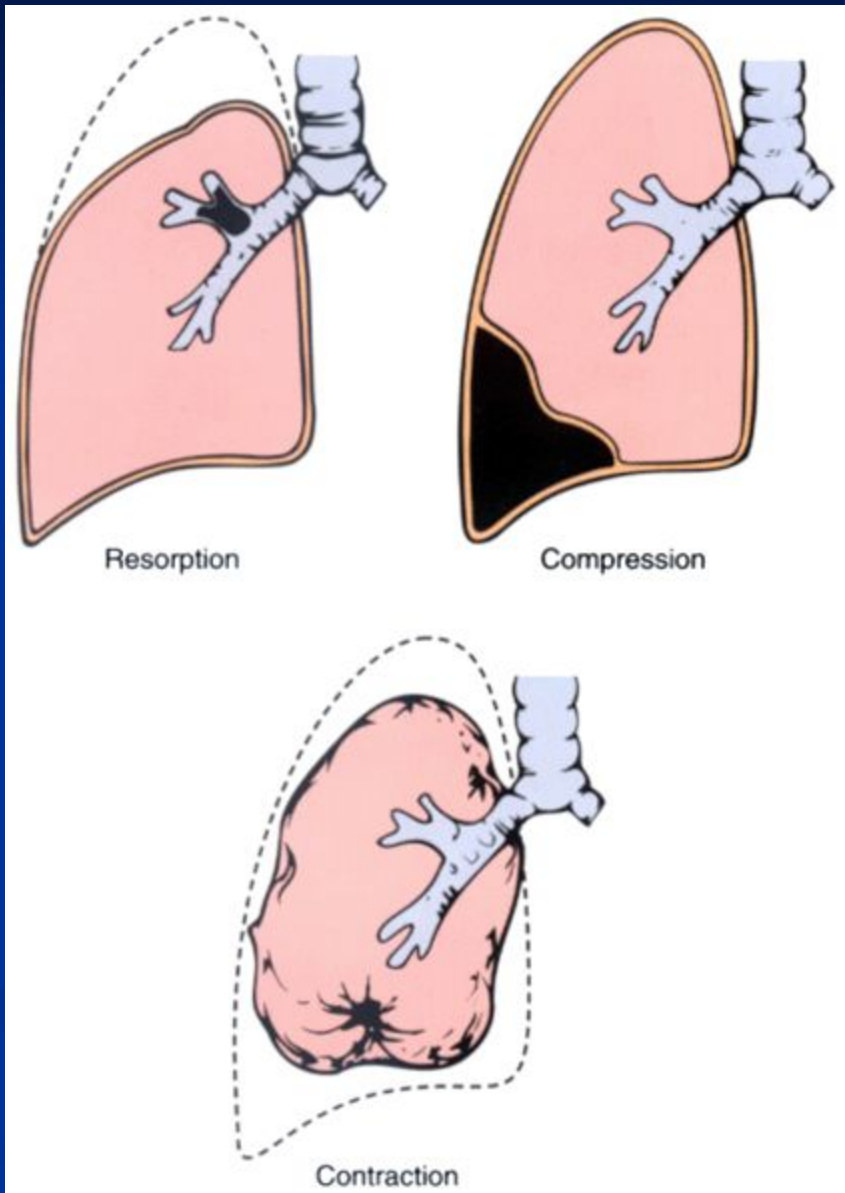
NORMAL



CXR

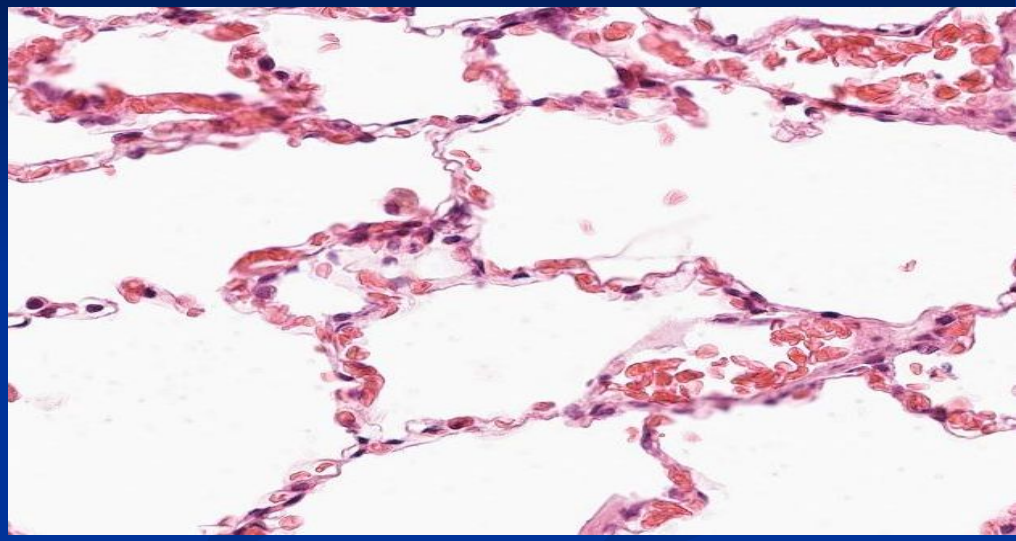
ATELECTASIS

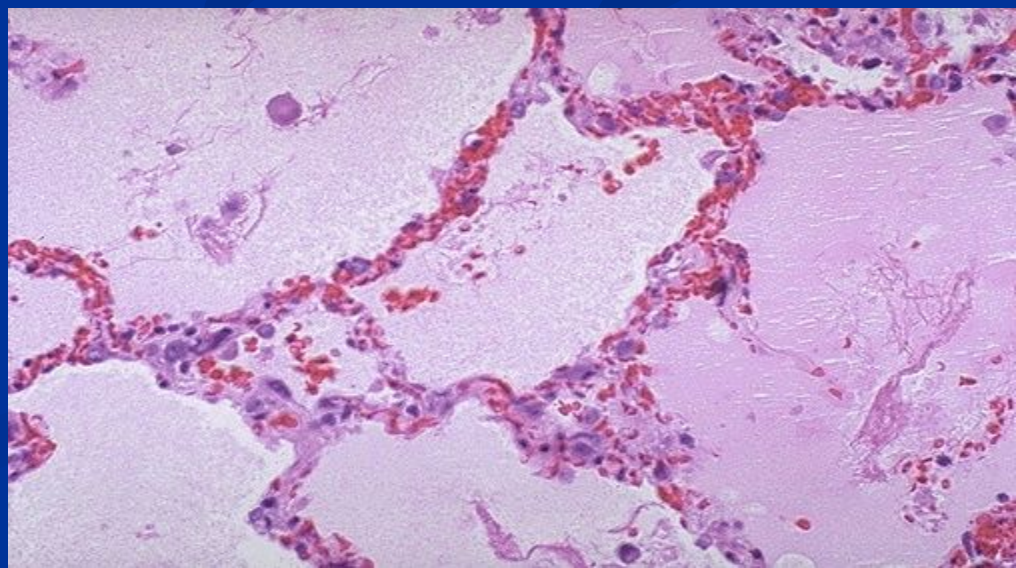
- INCOMPLETE EXPANSION
- COLLAPSE

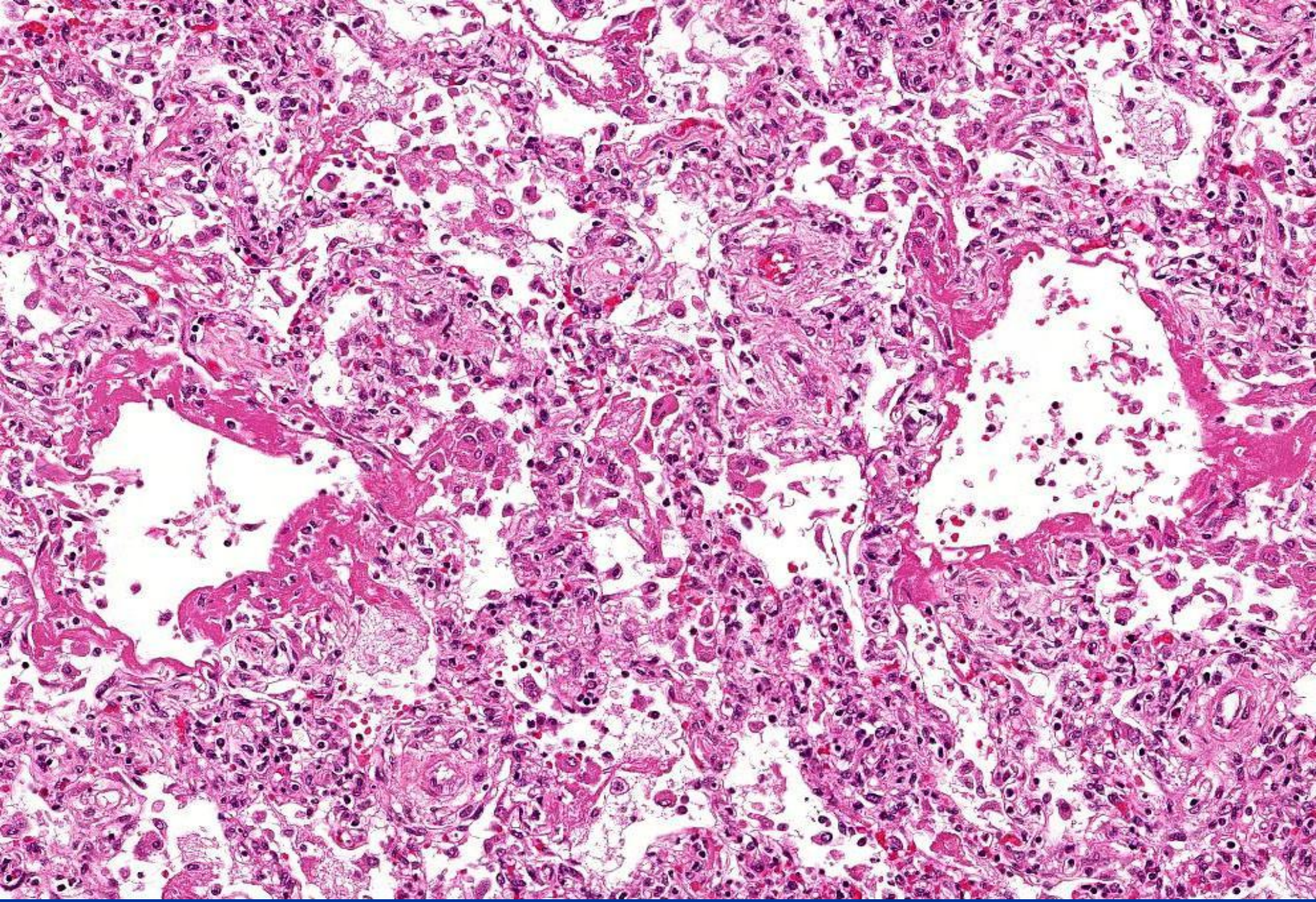


PULMONARY EDEMA

- IN-creased venous pressure
- DE-creased oncotic pressure
- Lymphatic obstruction
- Alveolar injury







ARDS

ACUTE INTERSTITIAL PNEUMONIA

- Think of it as ARDS with NO known etiology!

OBSTRUCTION v. RESTRICTION

- **OBSTRUCTION**
  - Air or blood?
  - Large or small?
  - Inspiration or Expiration?
  - **Obstruction is SMALL AIRWAY EXPIRATION**
    obstruction, i.e., wheezing
  - HYPEREXPANSION on CXR

- **RESTRICTION**
  - "Compliance"
  - "Infiltrative"
  - REDUCED lung VOLUME, DYSPNEA, CYANOSIS
  - **REDUCED GAS TRANSFER**
  - "GROUND GLASS" on CXR

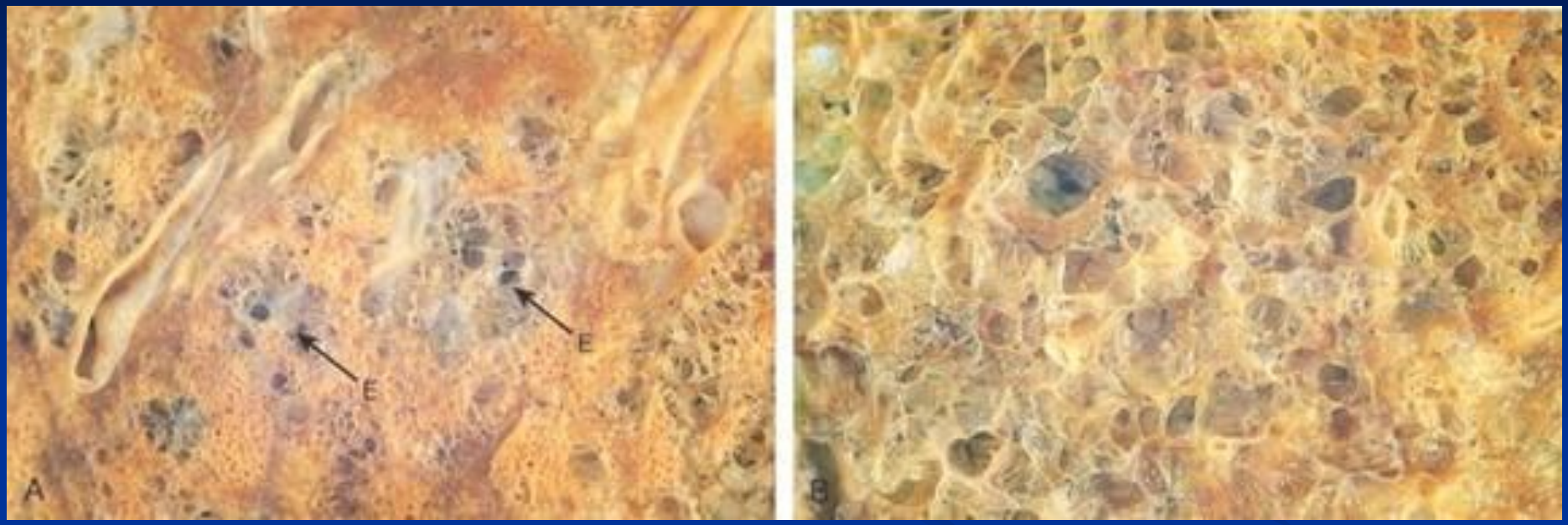
OBSTRUCTION (cOPD)

- **EMPHYSEMA** (almost always chronic)
- **CHRONIC BRONCHITIS** emphysema
- **ASTHMA**
- **BRONCHIECTASIS**

EMPHYSEMA

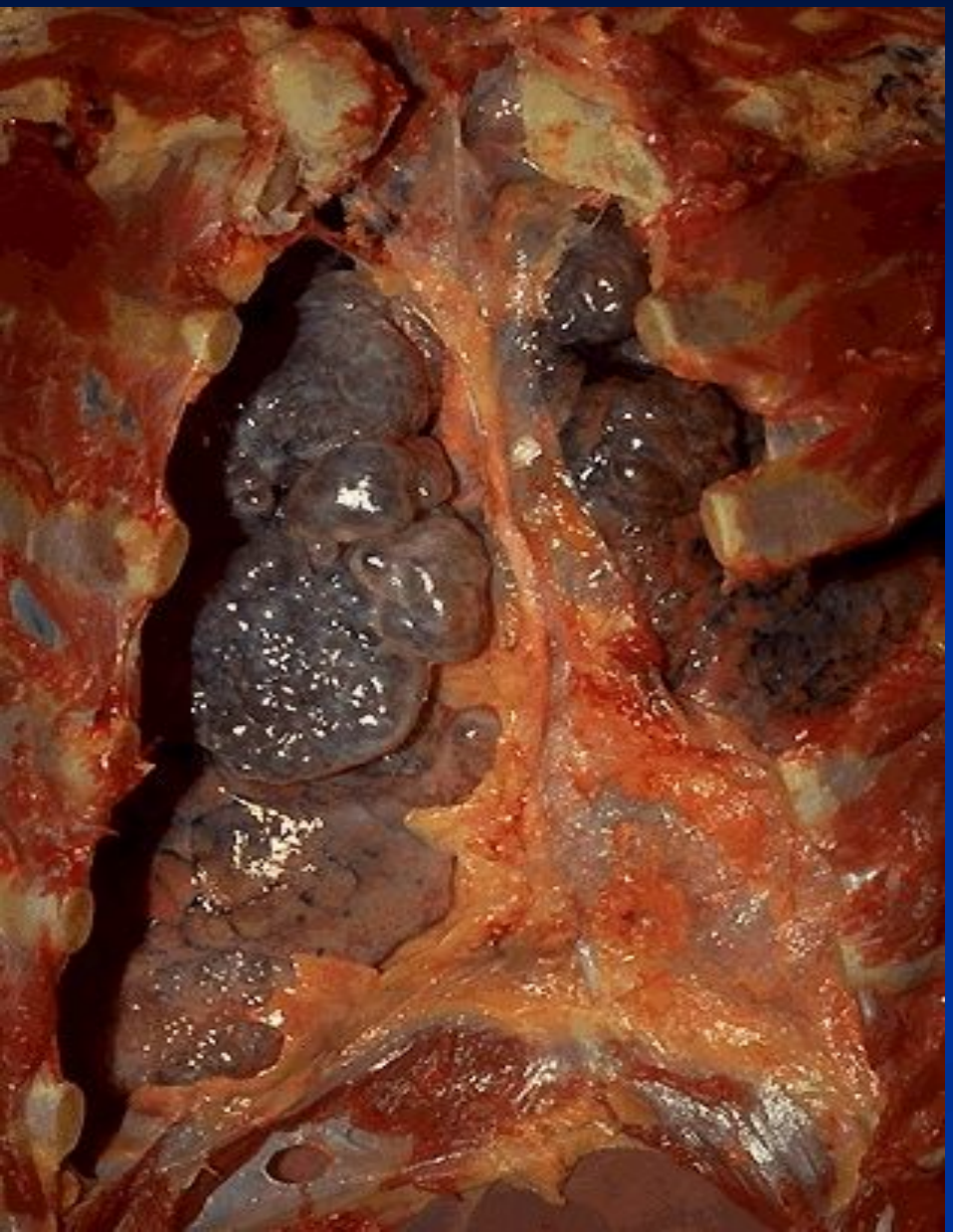
- COPD, or "END-STAGE" lung disease
- Centri-acinar, Pan-acinar, Paraseptal, Irregular
- Like cirrhosis, thought of as END-STAGE of multiple chronic small airway obstructive etiologies
- NON-specific
- IN-creased crepitance, BULLAE (BLEBS)
- Clinically linked to recurrent pneumonias, and progressive failure

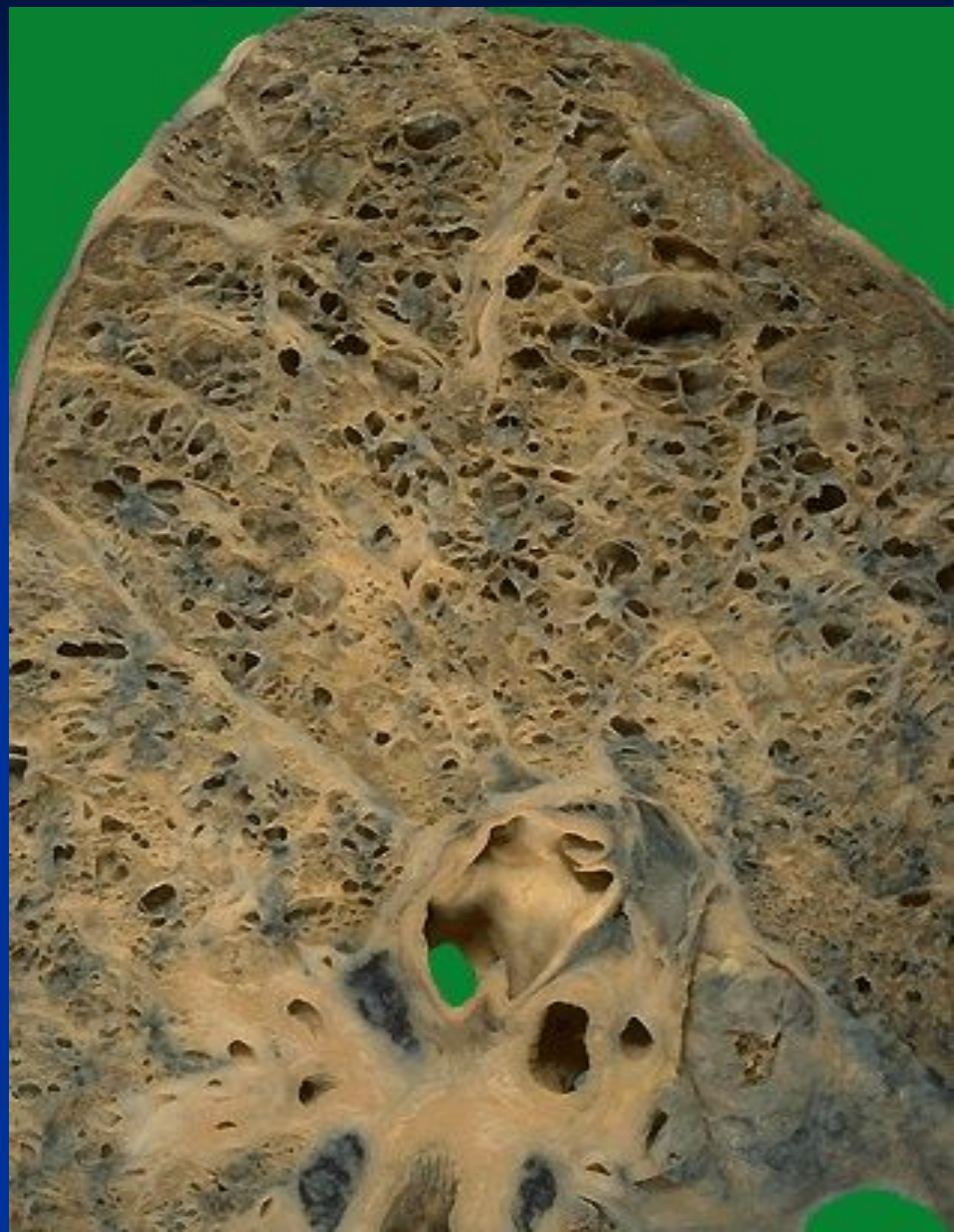
EMPHYSEMA



CENTRO-acinar **PAN-acinar**

Bullae, or "peripheral blebs" are hallmarks of chronic obstructive lung disease, COPD.

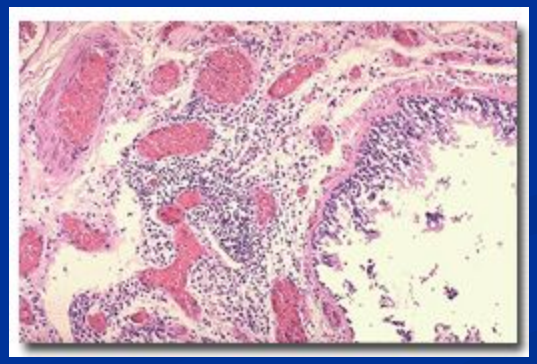




CHRONIC BRONCHITIS

- INHALANTS, POLLUTION, CIGARETTES
- CHRONIC COUGH
- CAN OFTEN PROGRESS TO EMPHYSEMA

- MUCUS hypersecretion, early, i.e. goblet cell increase
- CHRONIC bronchial inflammatory infiltrate



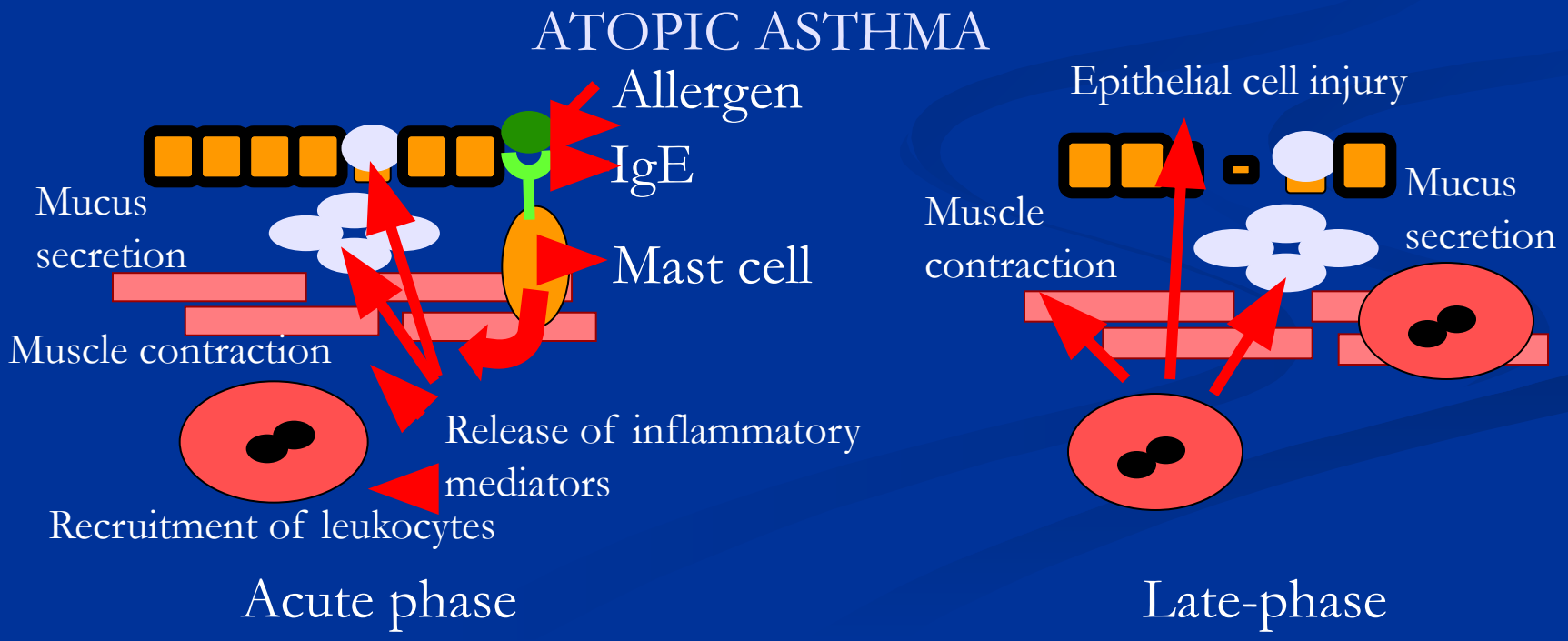
ASTHMA

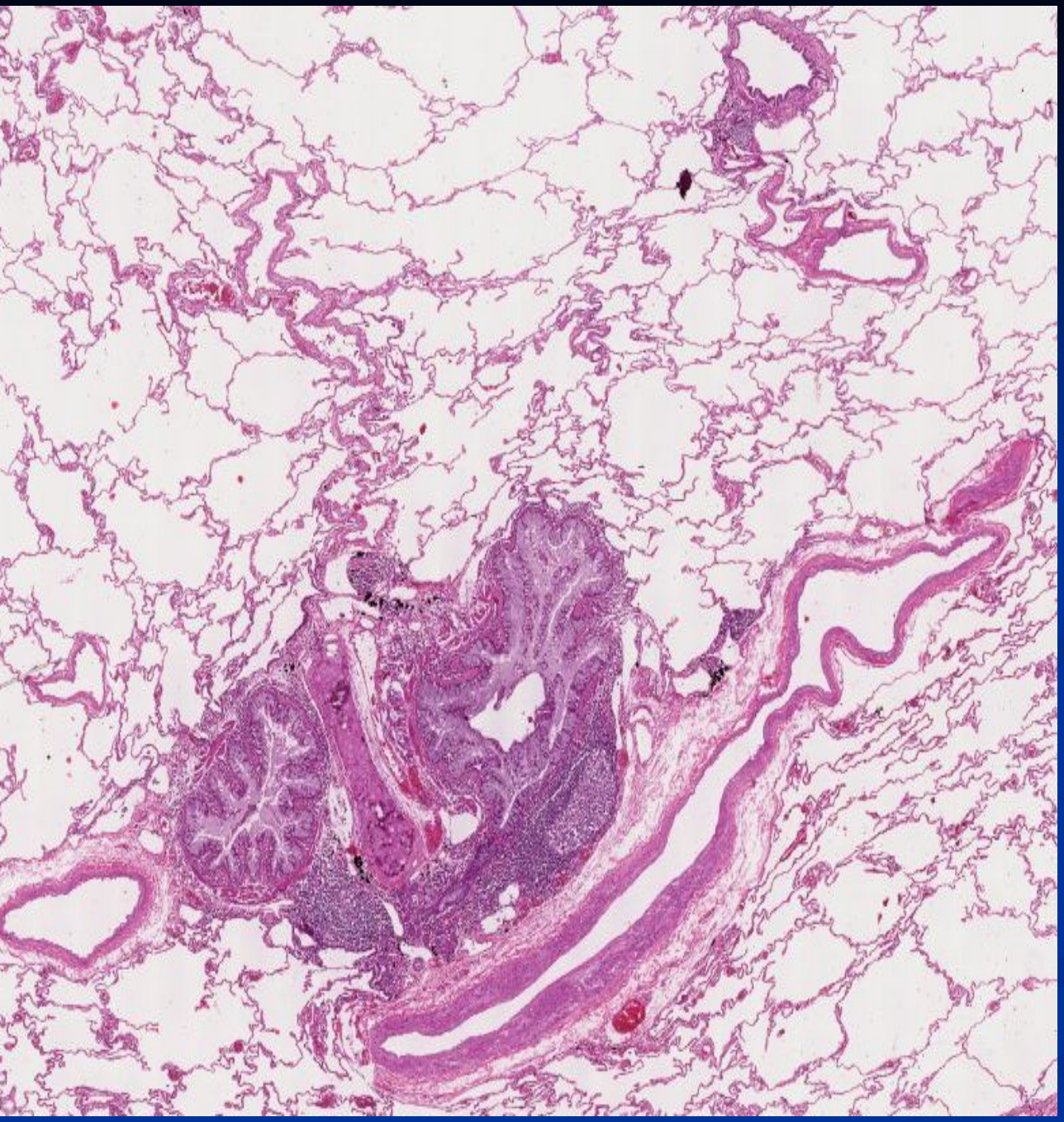
Similar to chronic bronchitis but:

- Wheezing is hallmark (bronchospasm, i.e. "wheezing")
- STRONG allergic role, i.e., eosinophils, IgE, allergens
- Often starting in CHILDHOOD
- ATOPIC (allergic) or NON-ATOPIC (infection)
- Chronic small airway obstruction and infection
- 1) Mucus hypersecretion with plugging, 2) lymphocytes/eosinophils, 3) lumen narrowing, 4) smooth muscle hypertrophy

Bronchial Asthma

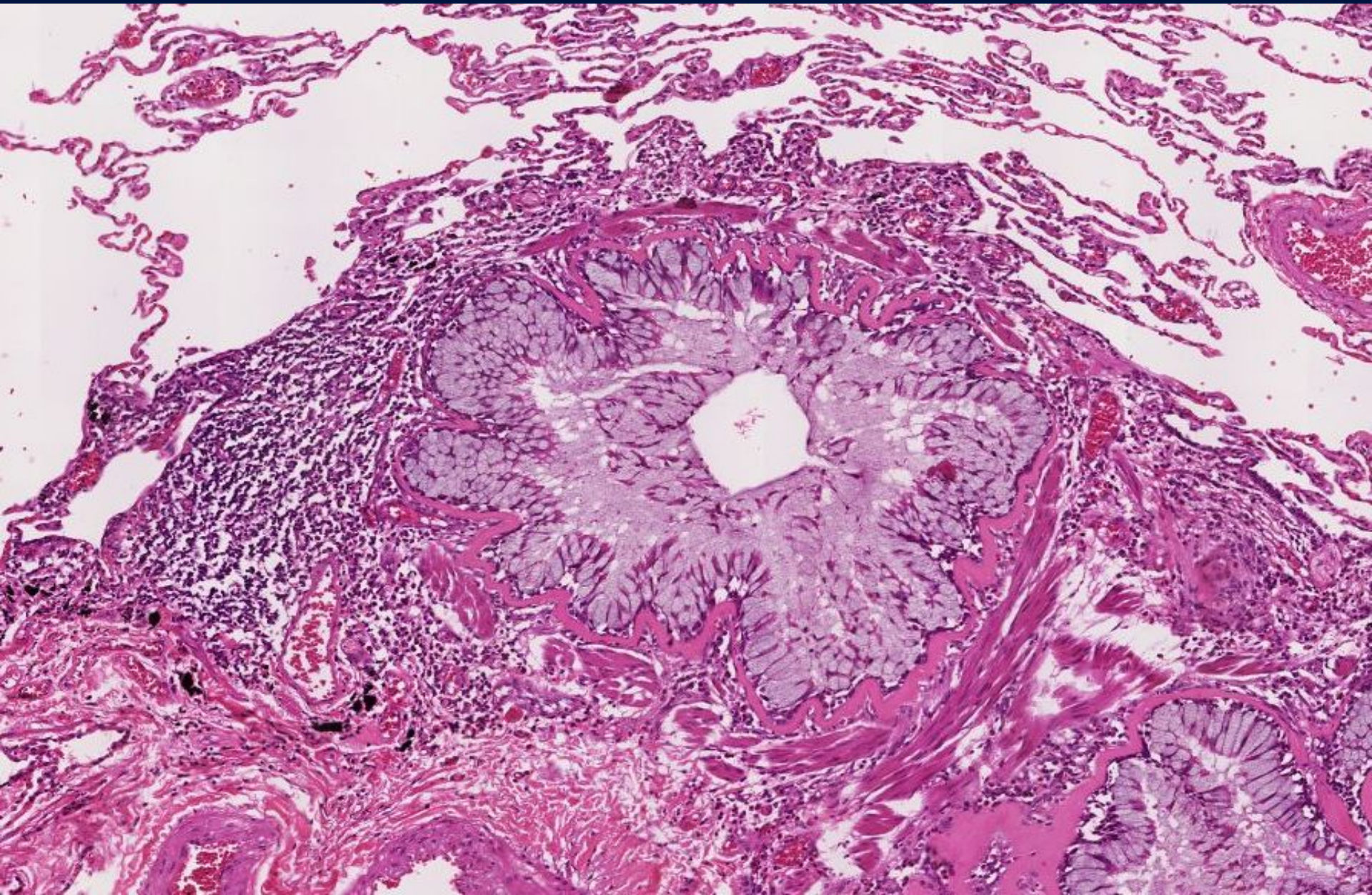
- **Chronic inflammatory disorder of the airways resulting in contraction of bronchial muscle**
- **Types**
  - **Extrinsic (atopic, allergic).**
    - **Allergens: food, pollen, dust, etc.**
  - **Intrinsic (non-atopic)**
    - **Initiated by infections, drugs, pollutants, chemical irritants**





Note the heavy inflammatory cell infiltrate around bronchioles and small bronchi.

What are the 4 classical histologic findings in bronchial asthma?

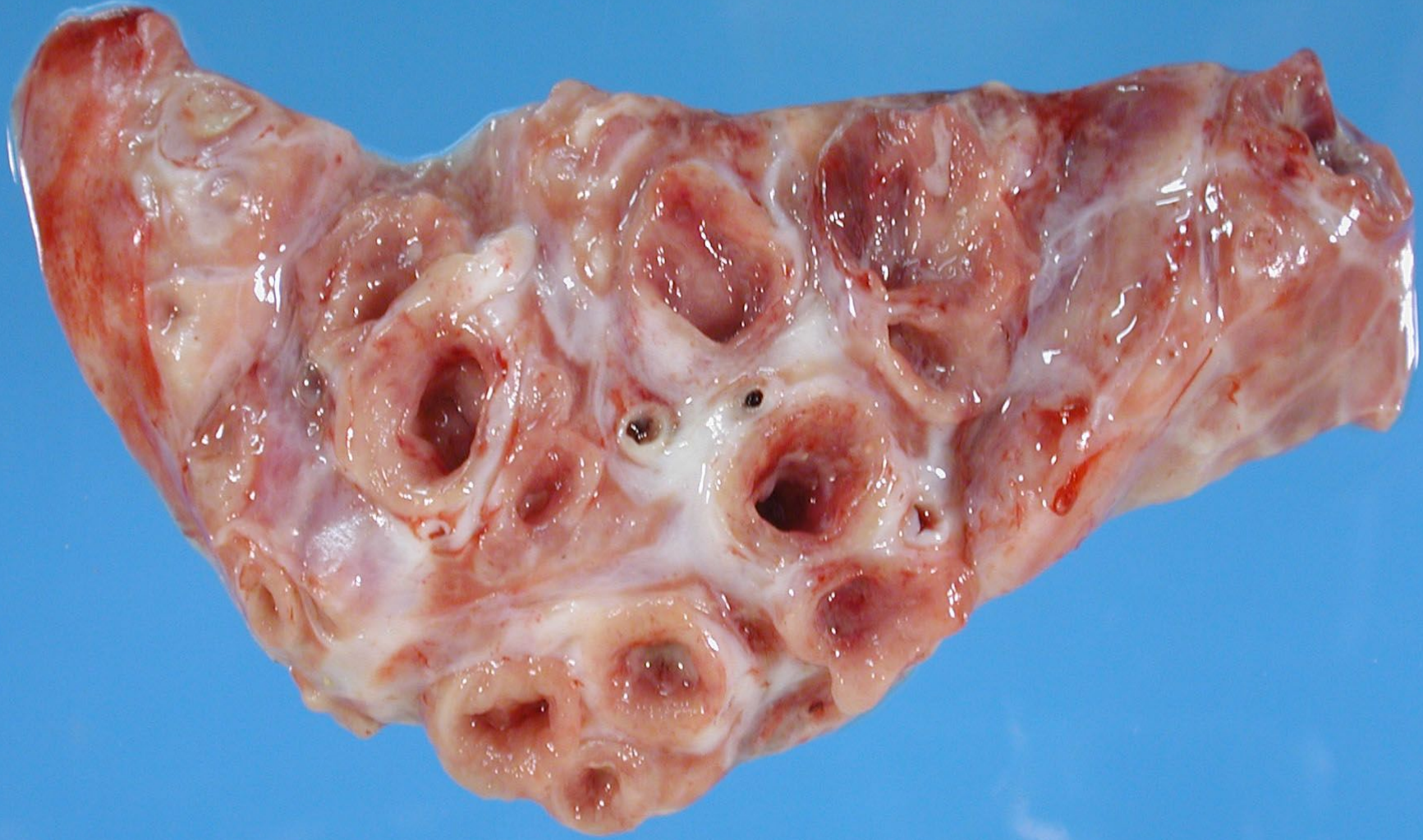


BRONCHIECTASIS

DILATATION of the BRONCHUS, associated with, often, necrotizing inflammation

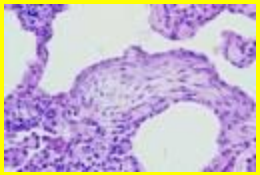
- **CONGENITAL**
- **TB, other bacteria, many viruses**
- **BRONCHIAL OBSTRUCTION (i.e., LARGE AIRWAY, NOT SMALL AIRWAY)**
- **Rheumatoid Arthritis, SLE, IBD (Inflammatory Bowel Disease)**

BRONCHIECTASIS

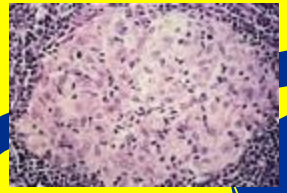


RESTRICTIVE (INFILTRATIVE)

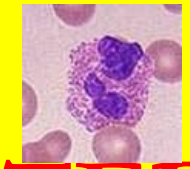
- REDUCED COMPLIANCE, reduced gas exchange)
- Are also DIFFUSE
- HETEROGENEOUS



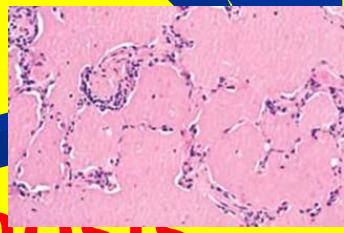
- FIBROSING



- GRANULOMATOUS
- EOSINOPHILIC



- SMOKING RELATED



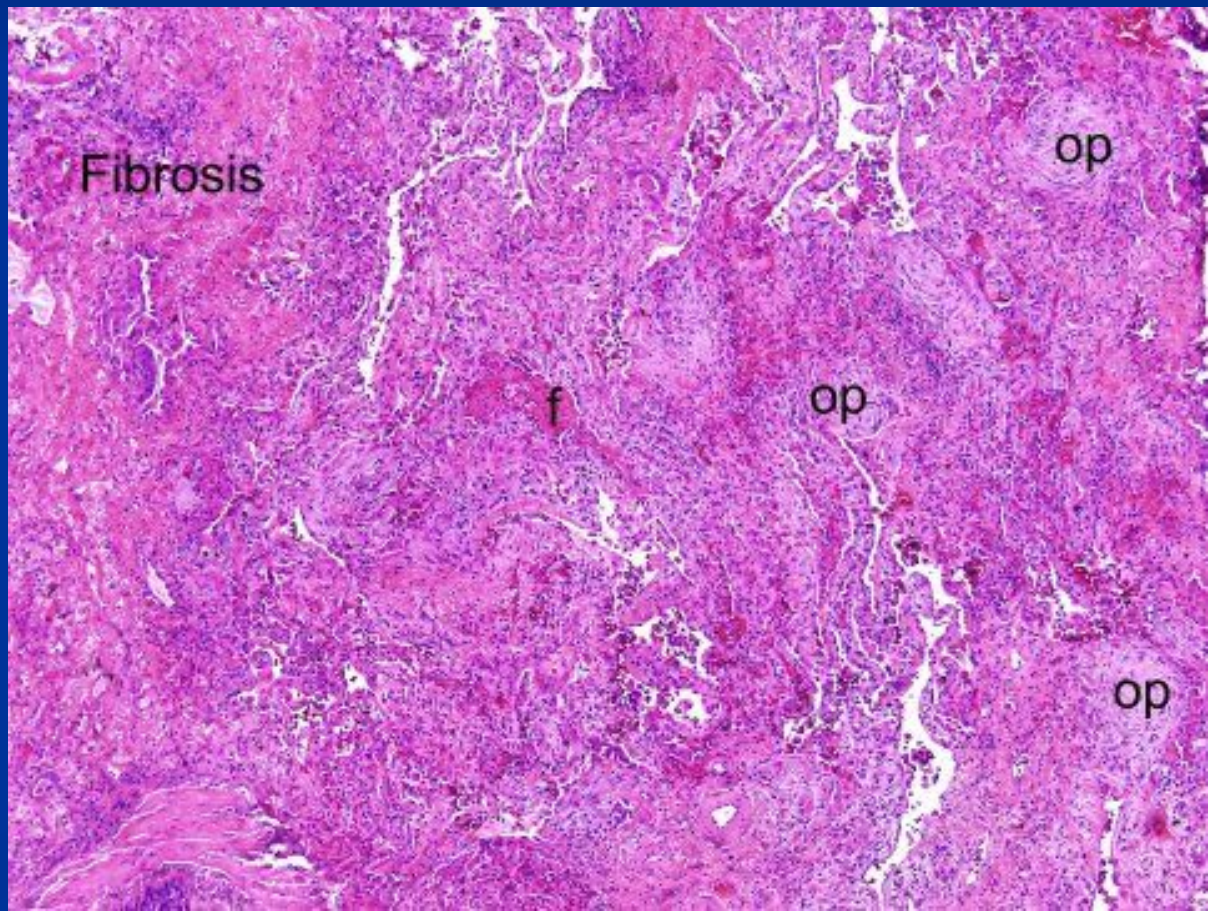
- PAP (Pulmonary Alveolar Proteinosis

FIBROSING

- "IDIOPATHIC" PULMONARY FIBROSIS (IPF)
- NONSPECIFIC INTERSTITIAL FIBROSIS
- "CRYPTOGENIC" ORGANIZING PNEUMONIA
- "COLLAGEN" VASCULAR DISEASES
- PNEUMOCONIOSES
- DRUG REACTIONS
- RADIATION CHANGES

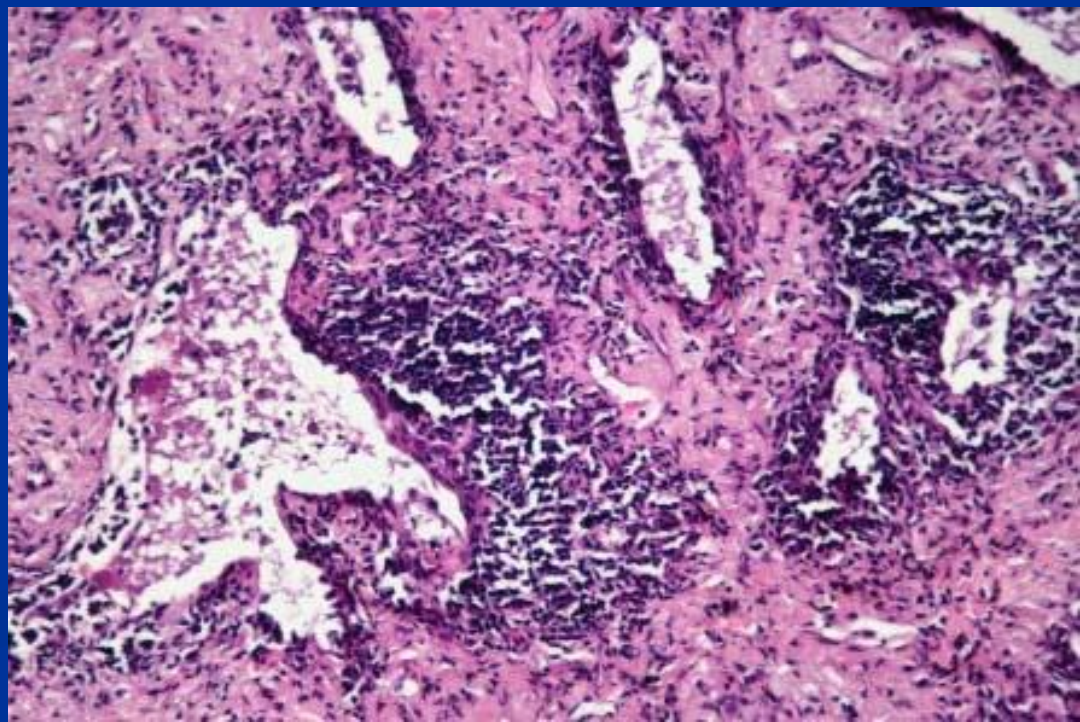
IPF (UIP)

- IDIOPATHIC, i.e., not from any usual caused, like lupus, scleroderma
- FIBROSIS



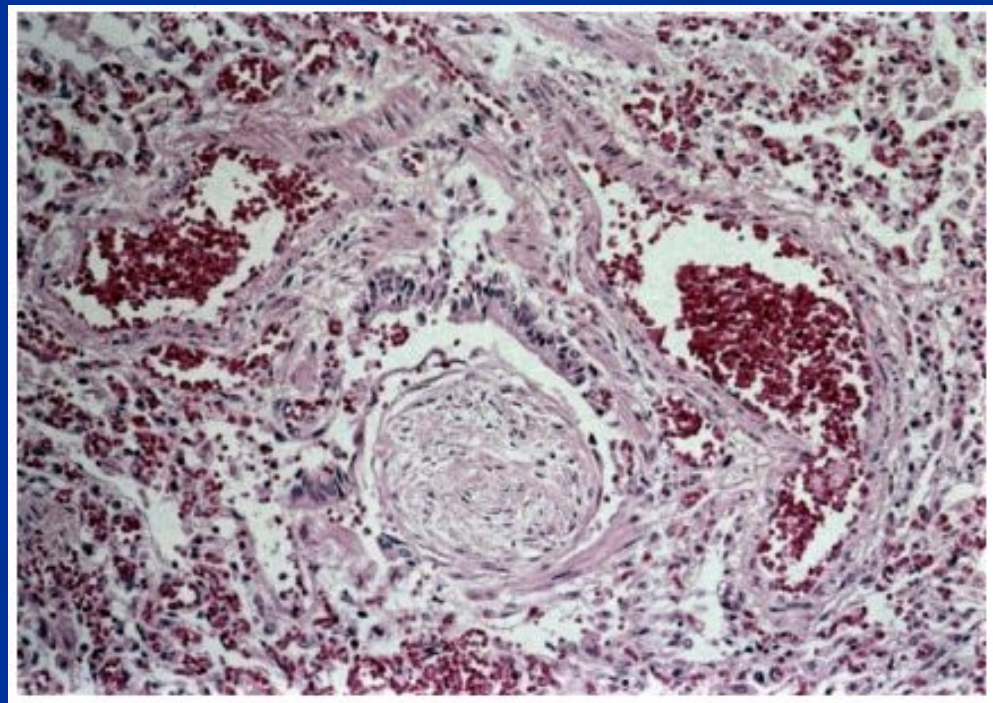
NON-SPECIFIC INTERSTITIAL PNEUMONIA

- **WASTEBASKET DIAGNOSIS, of ANY pneumonia (pneumonitis) of any known or unknown etiology**
  - **FIBROSIS**
  - **CELLULAR INFILTRATE (LYMPHS & PLASMA CELLS)**



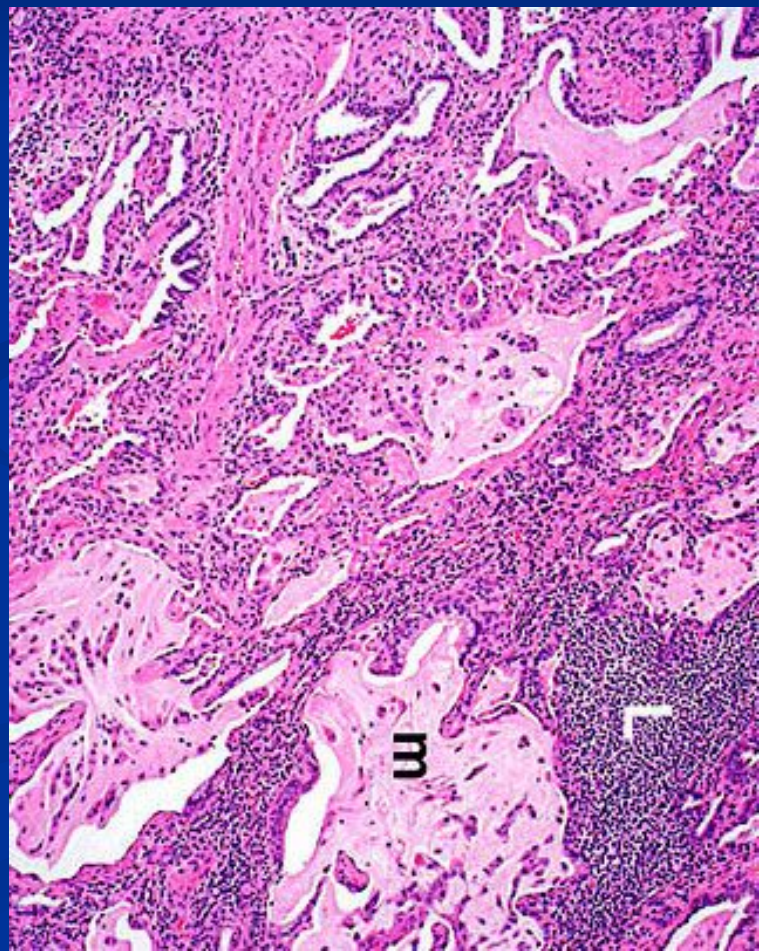
CRYPTOGENIC ORGANIZING PNEUMONIA (COP)

- IDIOPATHIC
- "BRONCHIOLITIS OBLITERANS"



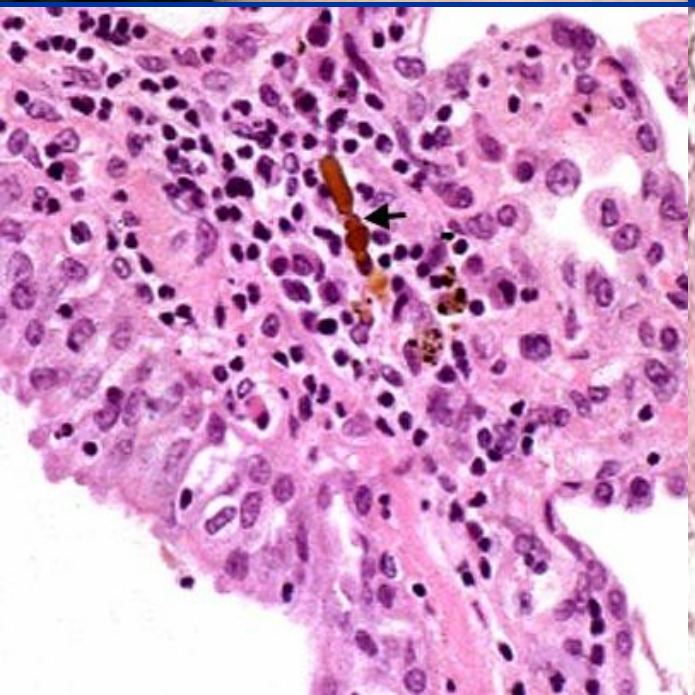
"COLLAGEN" VASCULAR DISEASES

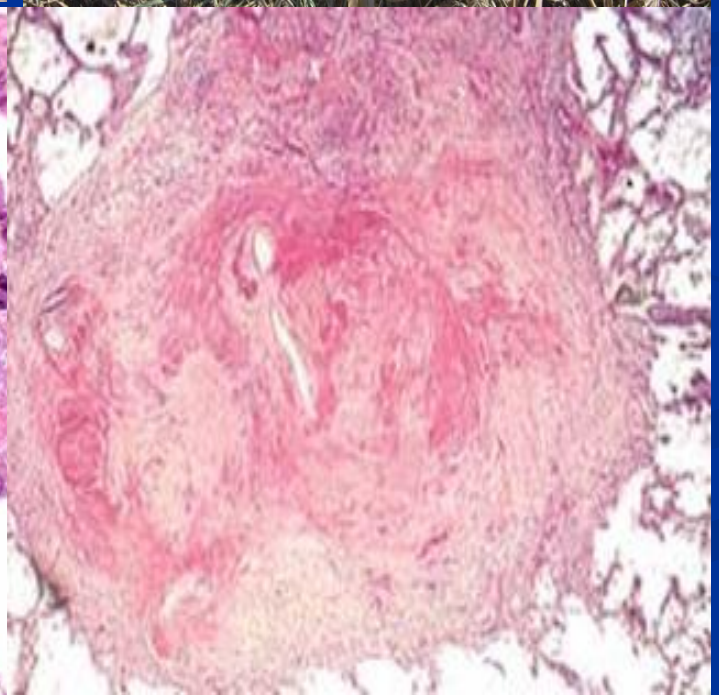
- Rheumatoid Arthritis
- SLE ("Lupus")
- Progressive Systemic Sclerosis (Scleroderma)



PNEUMOCONIOSES

- "OCCUPATIONAL"
- "COAL MINERS LUNG"
- DUST OR CHEMICALS OR ORGANIC MATERIALS
  - Coal (anthracosis)
  - Silica
  - Asbestos
  - Be, FeO, $BaSO_4$, CHEMO
  - HAY, FLAX, BAGASSE, INSECTICIDES, etc.





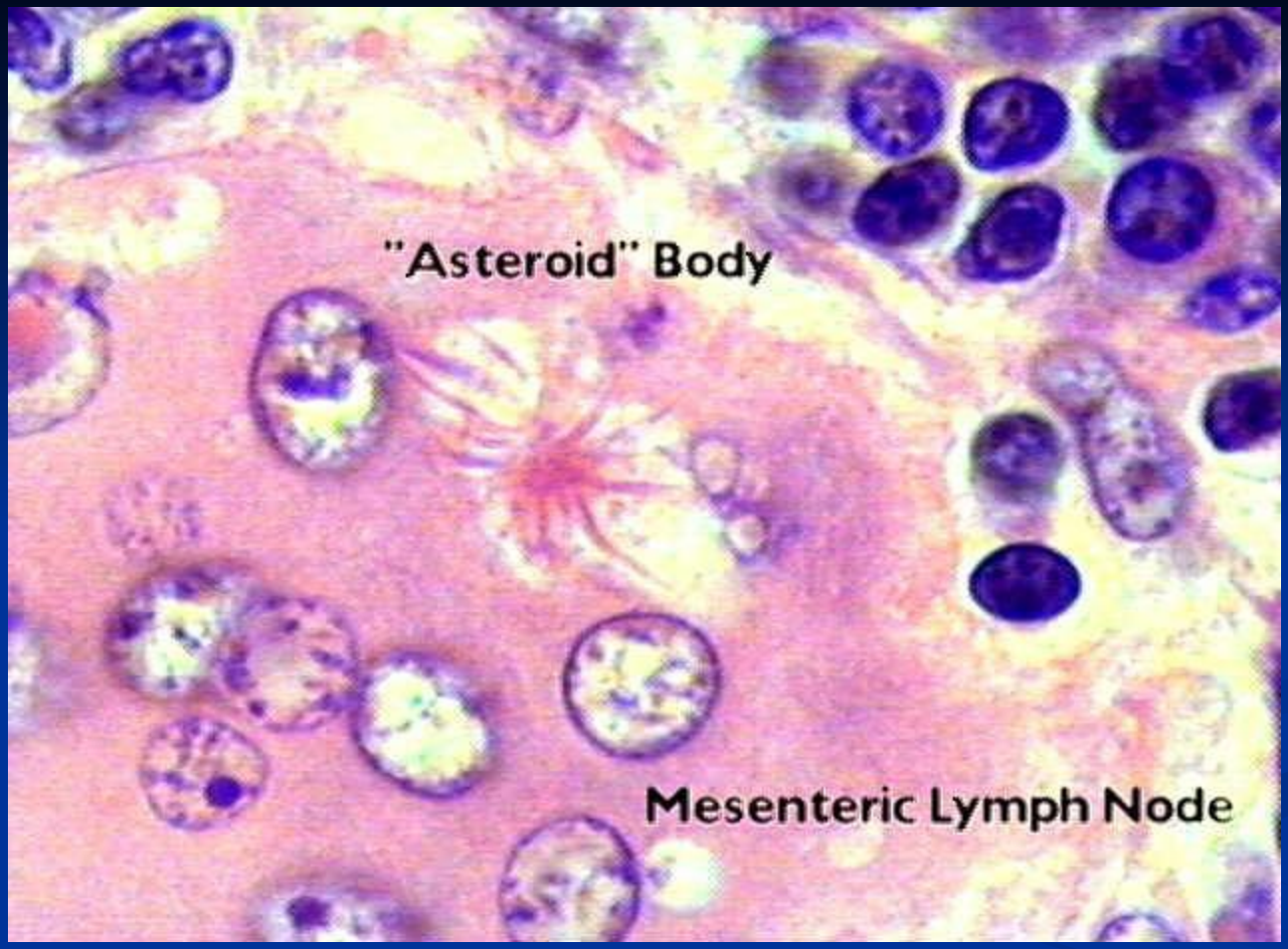
Coal, “bagasse”, asbestos, silica nodules, and asbestos, going clockwise.

GRANULOMATOUS

- **SARCOIDOSIS, i.e., NON-caseating granulomas (IDIOPATHIC)**
- **HYPERSENSITIVITY (DUSTS, bacteria, fungi, Farmer's Lung, Pigeon Breeder's Lung)**

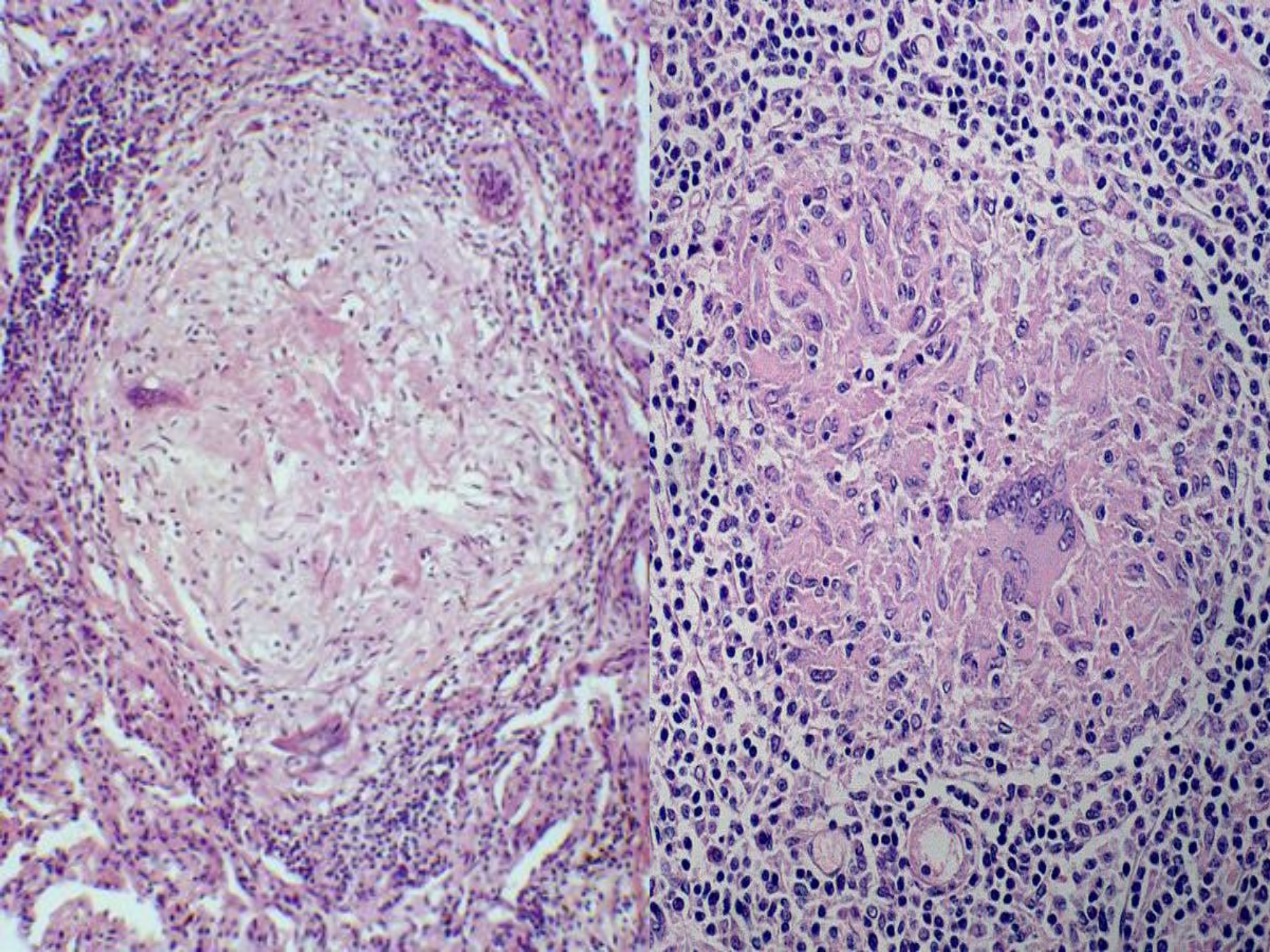
SARCOIDOSIS

- Mainly LUNG, but eye, skin or ANYWHERE
- UNKNOWN ETIOLOGY
- IMMUNE, GENETIC factors
- F>>M
- B>>W
- YOUNG ADULT BLACK WOMEN



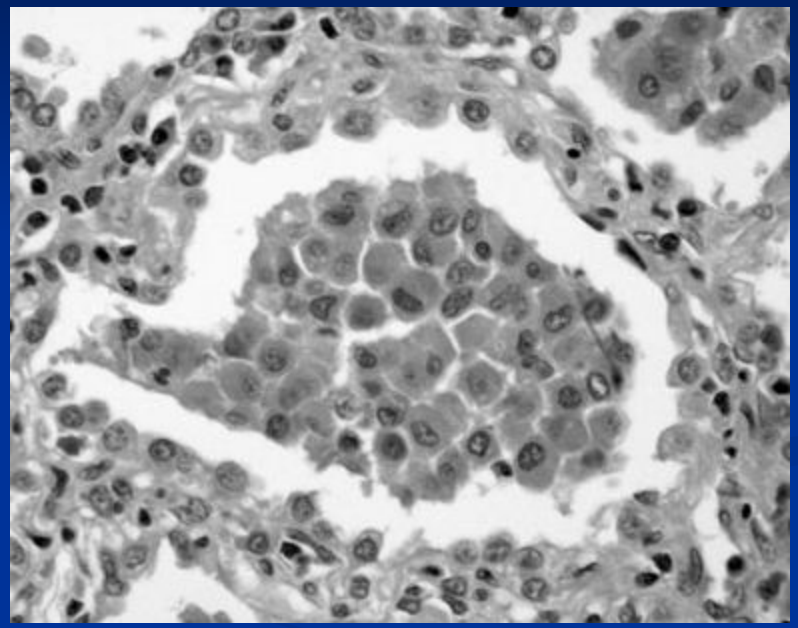
NON-Caseating Granulomas are the RULE

“Asteroid” bodies within these granulomas are virtually diagnostic



SMOKING RELATED

- **DIP (Desquamative Interstitial Pneumonia)**
  - M>>F
  - CIGARETTES
  - 100% Survival



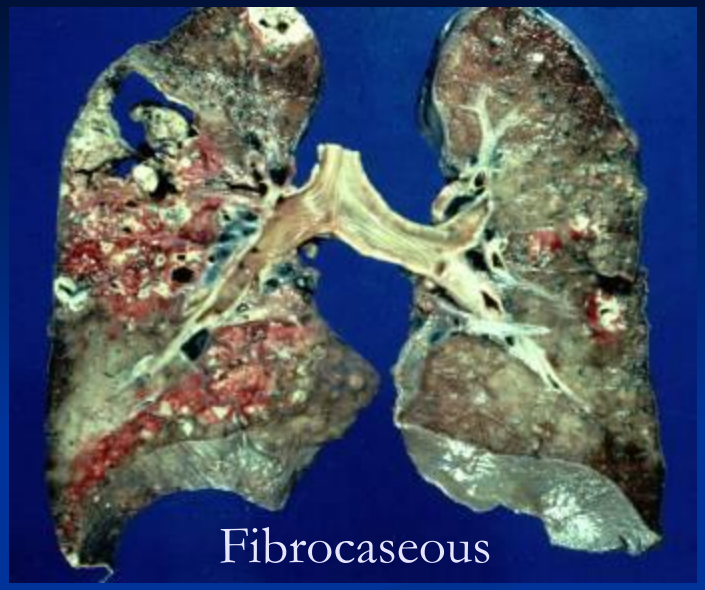
Alveolar Macrophages

Pulmonary tuberculosis

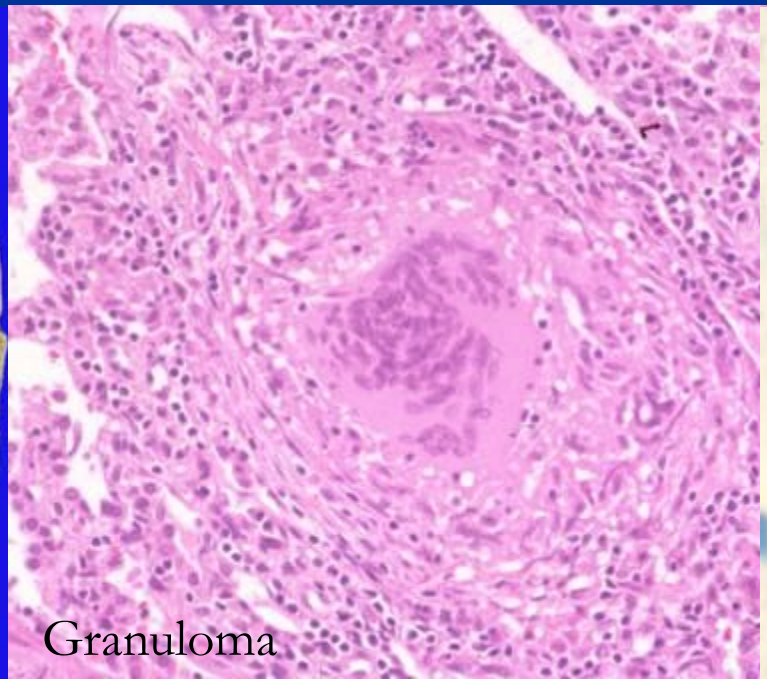
- Caused by *Mycobacterium tuberculosis*.
- Transmitted through inhalation of infected droplets
- Primary
  - Single granuloma within parenchyma and hilar lymph nodes (Ghon complex).
    - Infection does not progress (most common).
    - Progressive primary pneumonia
    - Miliary dissemination (blood stream).

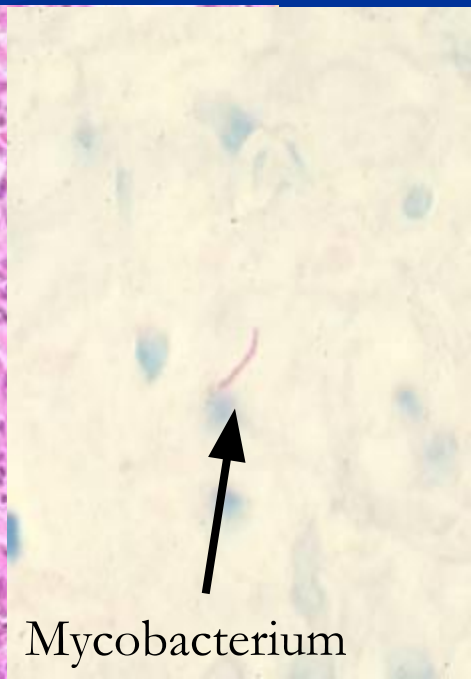
Pulmonary tuberculosis

- Secondary
  - Infection (mostly through reactivation) in a previously sensitized individual.
  - Pathology
    - Cavitary fibrocaseous lesions
    - Bronchopneumonia
    - Miliary TB


Fibrocaseous


Miliary


Granuloma

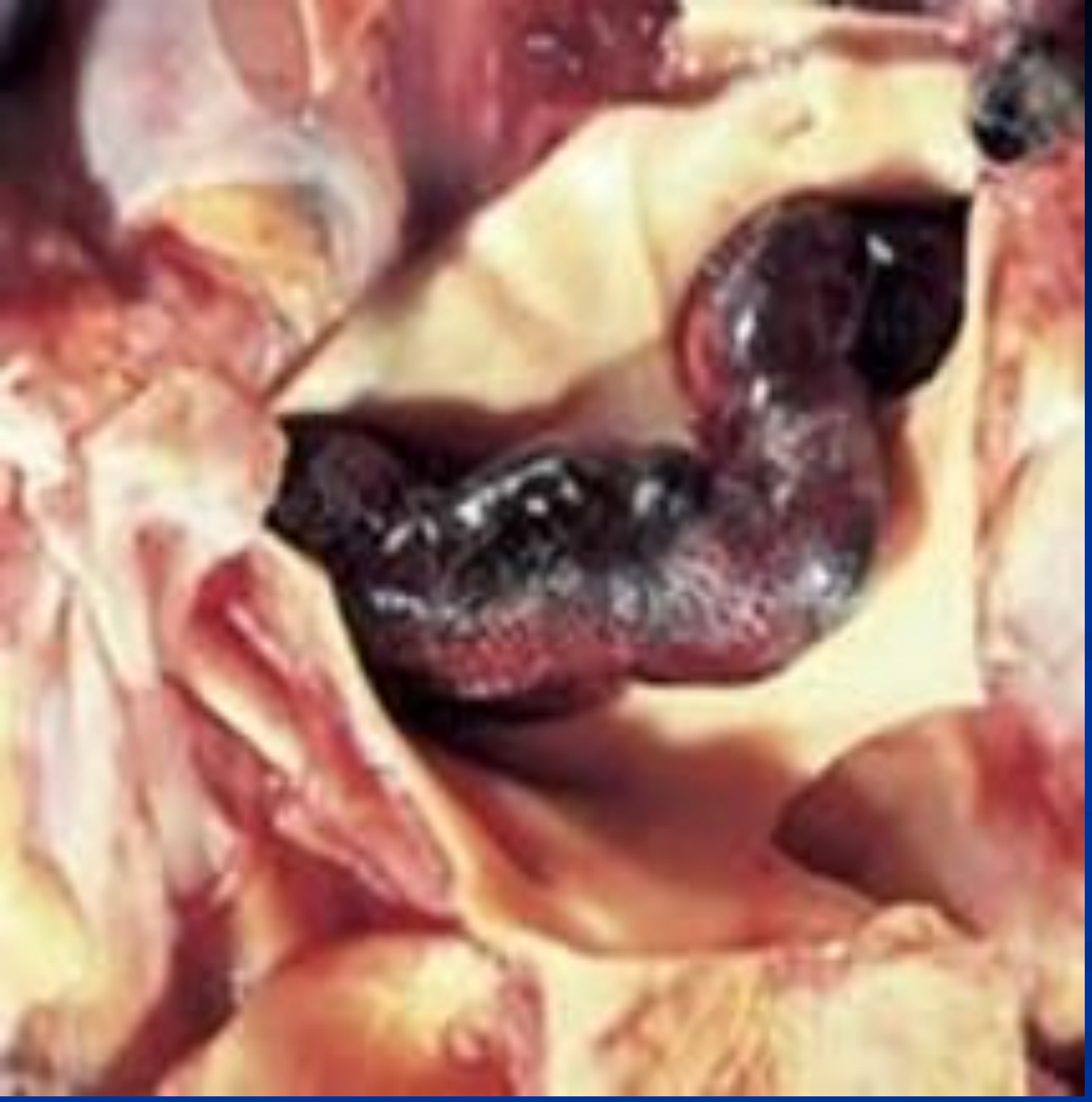

Mycobacterium

VASCULAR PULMONARY DISEASES

- **PULMONARY EMBOLISM** (with or usually WITHOUT infarction)
- **PULMONARY HYPERTENSION**, leading to cor pulmonale
- **HEMORRHAGIC SYNDROMES**
  - **GOODPASTURE SYNDROME**
  - **HEMOSIDEROSIS**, idiopathic
  - **WEGENER GRANULOMATOSIS**

P.E.

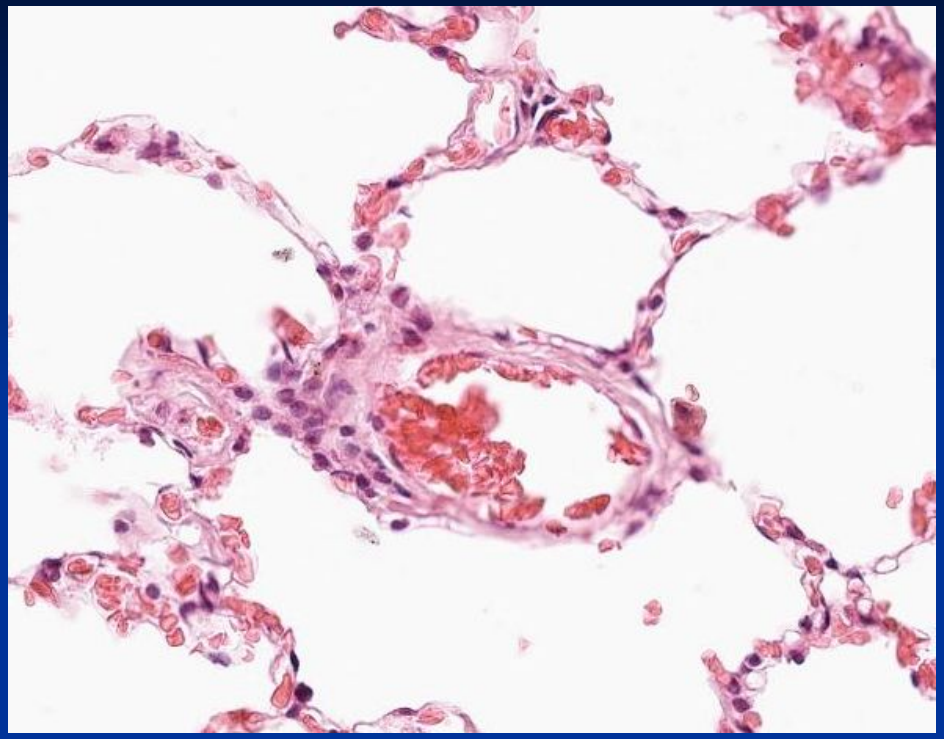
- Usually secondary to debilitated states with immobilization, or following surgery
- Usually deep leg and deep pelvic veins (DVT), NOT superficial veins
- Follows Virchow's triad, i.e., 1) flow problems, 2) endothelial disruption, 3) hypercoagulabilty
- Usually do NOT infarct, usually ventilate
- When they DO infarct, the infarct is hemorrhagic
- Decreased PO2, acute chest pain, V/Q MIS-match
- DX: Chest CT, V/Q scan, angiogram
- RX: short term heparin, then long term coumadin



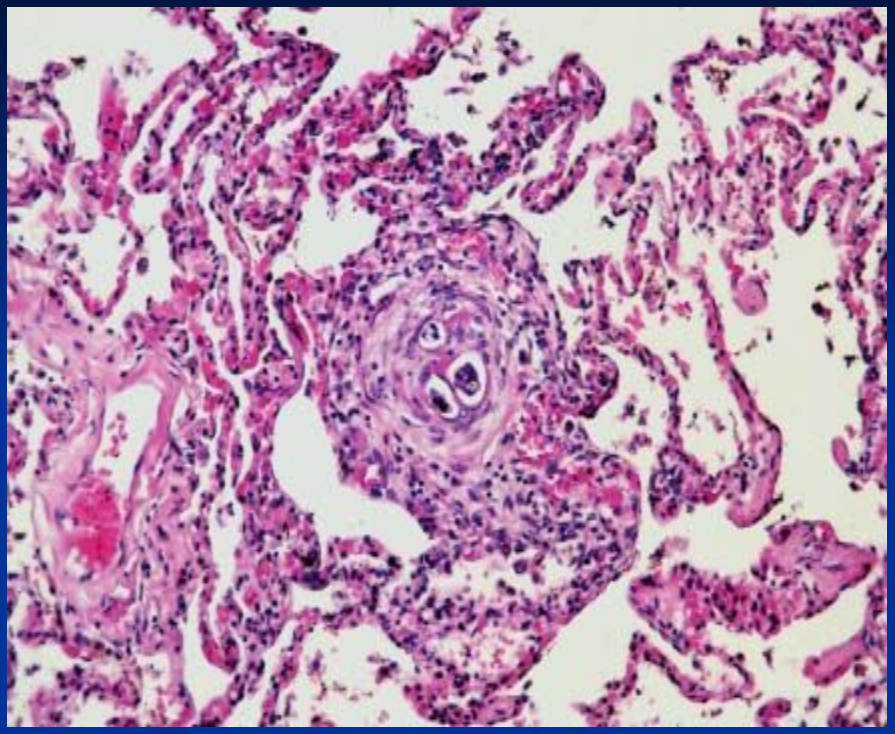
GROSS
“saddle”
embolism

PULMONARY HYPERTENSION

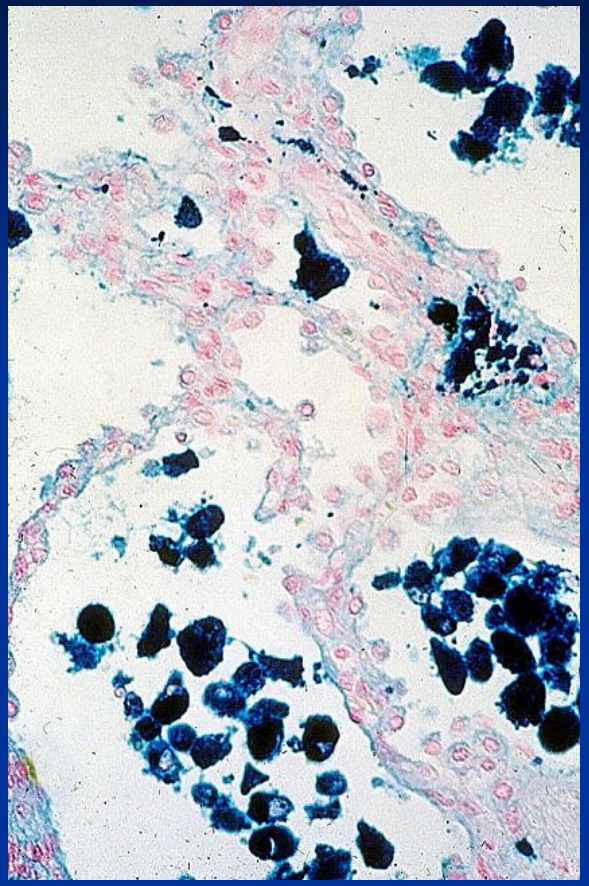
- COPD, C"I"PD (vicious cycle)
- CHD (Congenital HD, increased left atrial pressure)
- Recurrent PEs
- Autoimmune, e.g., PSS (Scleroderma), i.e., fibrotic pulmonary vasculature



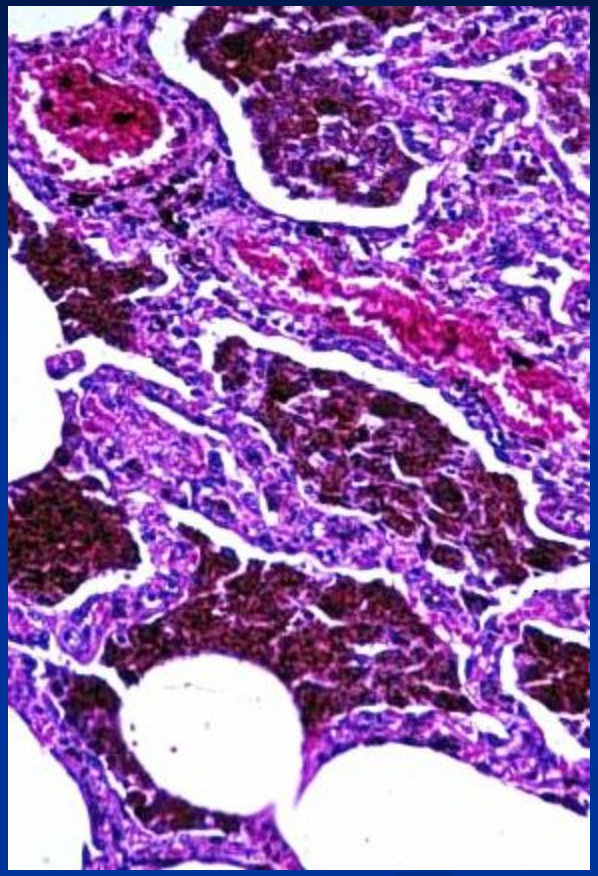
NORMAL pulmonary arteriole



VERY thickened arteriole in pulmonary hypertension

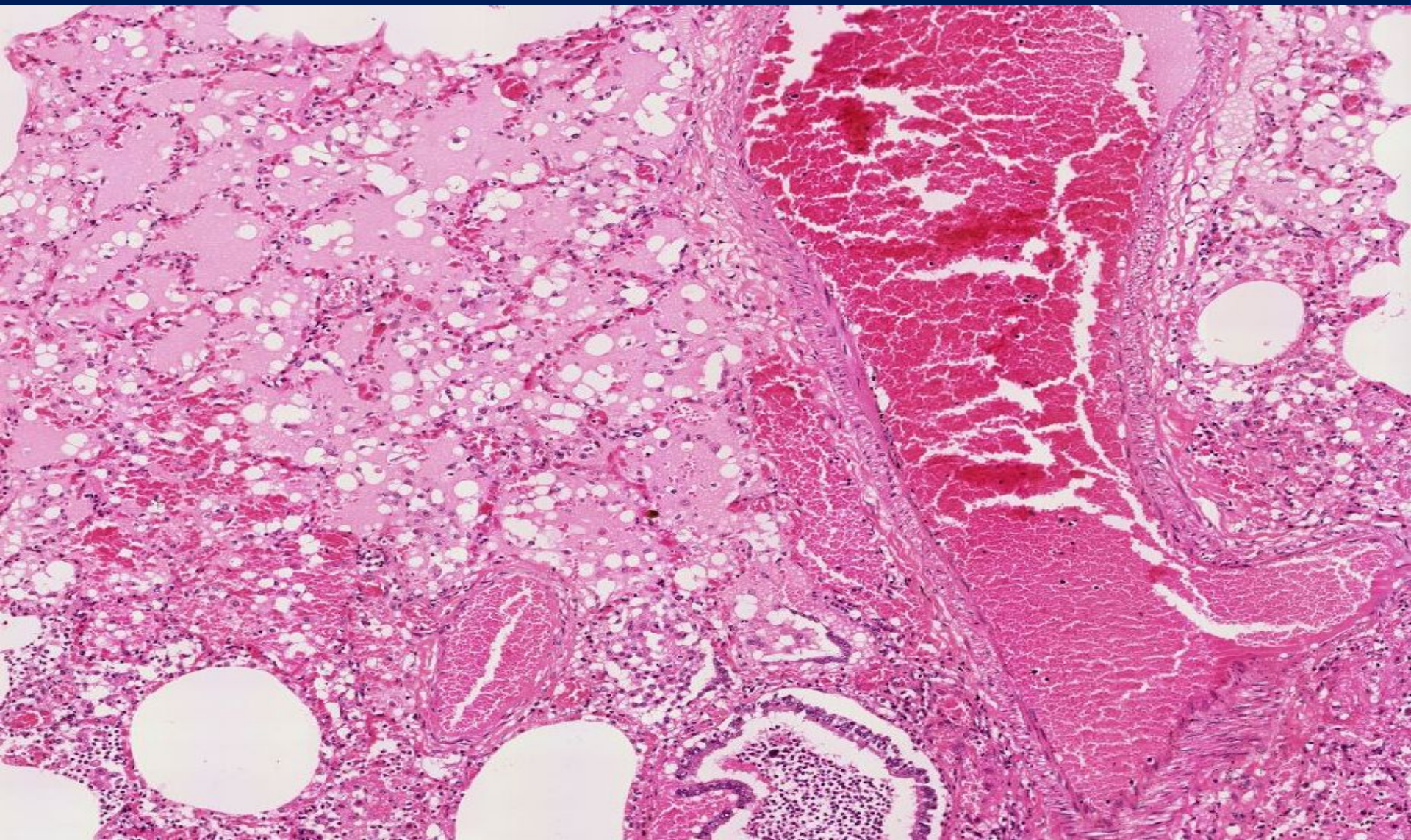


CHF, **CHRONIC**



IDIOPATHIC PULMONARY HEMOSIDEROSIS

PNEUMONIA



PULMONARY INFECTIONS

COMMUNITY-ACQUIRED BACTERIAL ACUTE PNEUMONIAS
- Streptococcus Pneumoniae
- Haemophilus Influenzae
- Moraxella Catarrhalis
- Staphylococcus Aureus
- Klebsiella Pneumoniae
- Pseudomonas Aeruginosa
- Legionella Pneumophila

COMMUNITY-ACQUIRED ATYPICAL (VIRAL AND MYCOPLASMAL) PNEUMONIAS
- Morphology.
- Clinical Course.
- Influenza Infections
- Severe Acute Respiratory Syndrome (SARS)

NOSOCOMIAL PNEUMONIA

ASPIRATION PNEUMONIA

LUNG ABSCESS
- Etiology and Pathogenesis.

CHRONIC PNEUMONIA
- Histoplasmosis, Morphology
- Blastomycosis, Morphology
- Coccidioidomycosis, Morphology

PNEUMONIA IN THE IMMUNOCOMPROMISED HOST

PULMONARY DISEASE IN HUMAN IMMUNODEFICIENCY VIRUS INFECTION

BASIC CONSIDERATIONS

- PNEUMONIA vs. PNEUMONITIS
- DIFFERENTIATION from INJURIES, OBSTRUCTIVE DISEASES, RESTRICTIVE DISEASES, VASCULAR DISEASES
- DIFFERENTIATION FROM NEOPLASMS
- CLASSICAL STAGES of INFLAMMATION
- LOBAR- vs. BRONCHO-
- INTERSTITIAL vs. ALVEOLAR
- COMMUNITY vs. NOSOCOMIAL
- ETIOLOGIC AGENTS vs. HOST IMMUNITY
- 2 PRESENTING SYMPTOMS
- 2 DIAGNOSTIC METHODS
- ANY ORGANISM CAN CAUSE PNEUMONIA!!!

PREDISPOSING FACTORS

- LOSS OF COUGH REFLEX
- DIMINISHED MUCIN or CILIA FUNCTION
- ALVEOLAR MACROPHAGE INTERFERENCE
- VASCULAR FLOW IMPAIRMENTS
- BRONCHIAL FLOW IMPAIRMENTS

Although pneumonia is one of the most common causes of death, it usually does **NOT** occur in healthy people spontaneously

Classifications of PNEUMONIAS

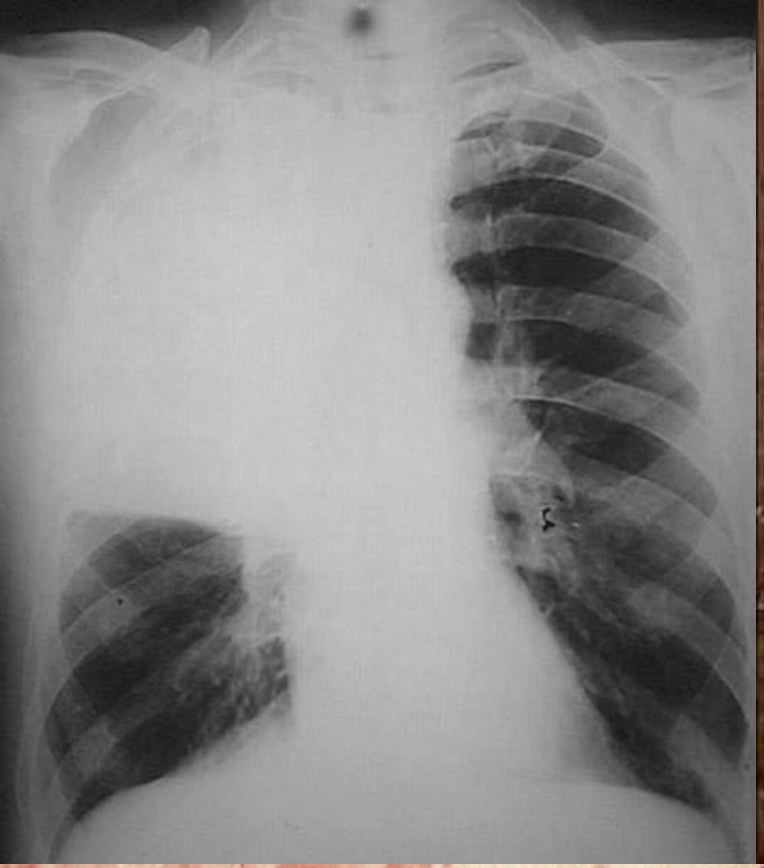
- COMMUNITY ACQUIRED
- COMMUNITY ACQUIRED, ATYPICAL
- NOSOCOMIAL
- ASPIRATION
- CHRONIC
- NECROTIZING/ABSCESS FORMATION
- PNEUMONIAS in IMMUNOCOMPROMISED HOSTS

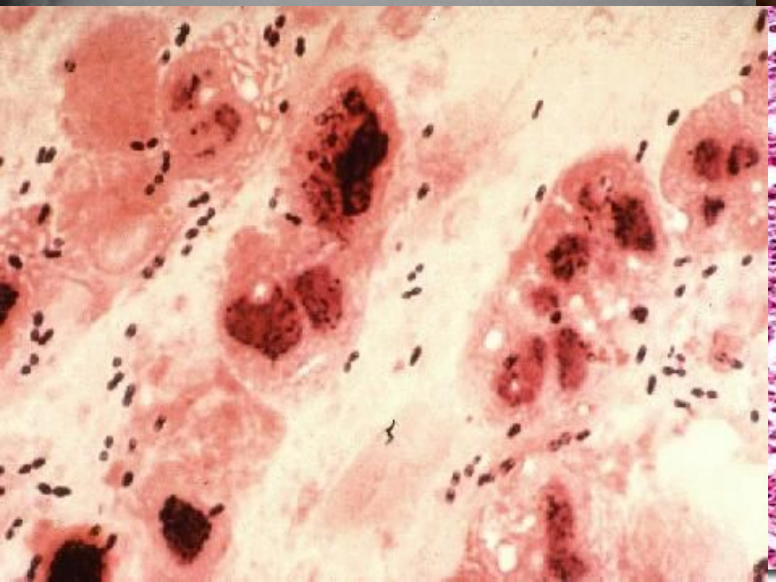
COMMUNITY ACQUIRED

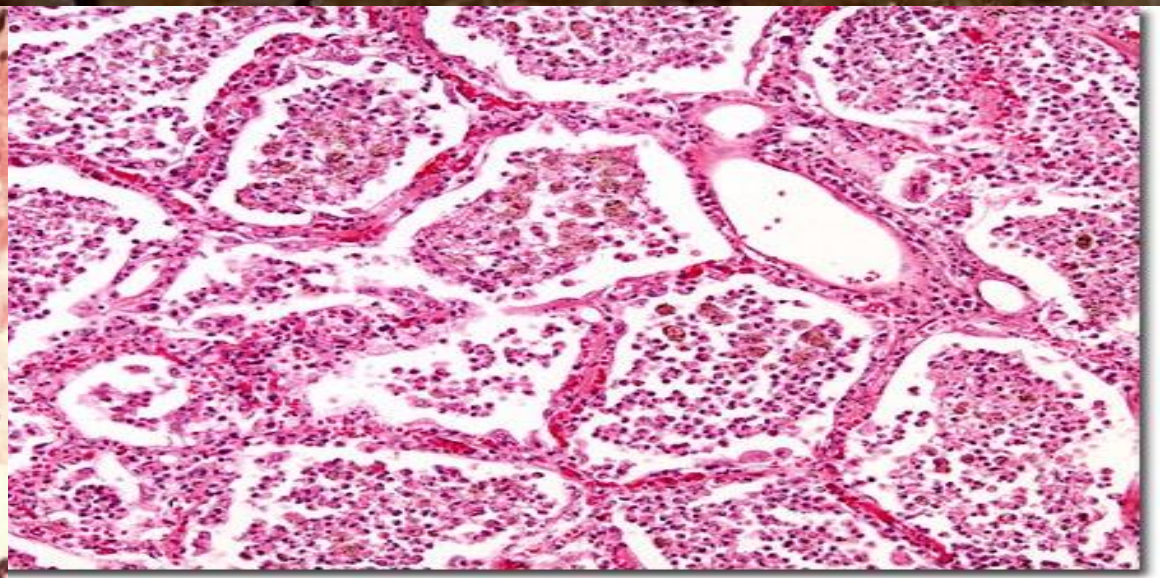
- STREPTOCOCCUS PNEUMONIAE (i.e., "diplococcus")
- HAEMOPHILUS INFLUENZAE ("H-Flu")
- MORAXELLA
- STAPHYLOCOCCUS (STAPH)
- KLEBSIELLA PNEUMONIAE
- PSEUDOMONAS AERUGINOSA
- LEGIONELLA PNEUMOPHILIA

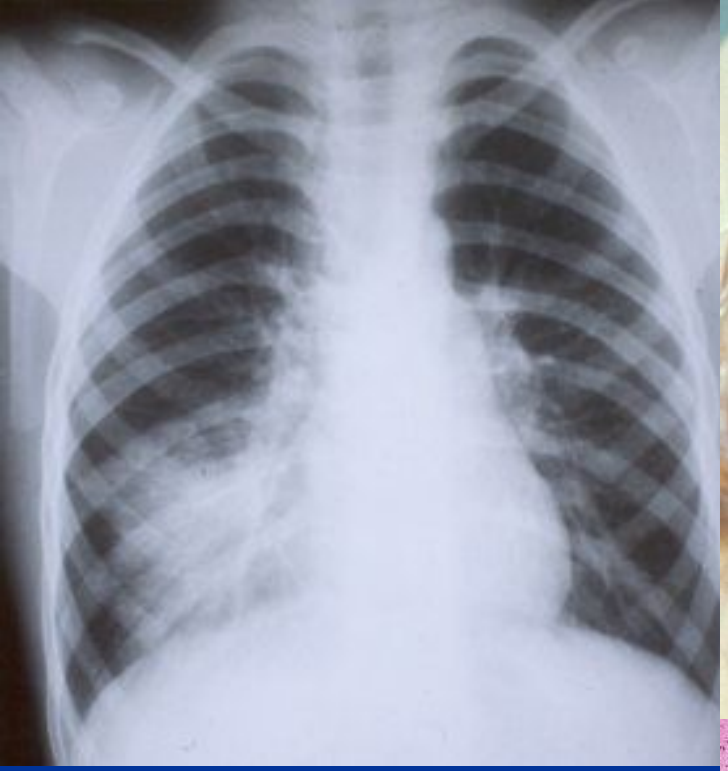
STREPTOCOCCUS

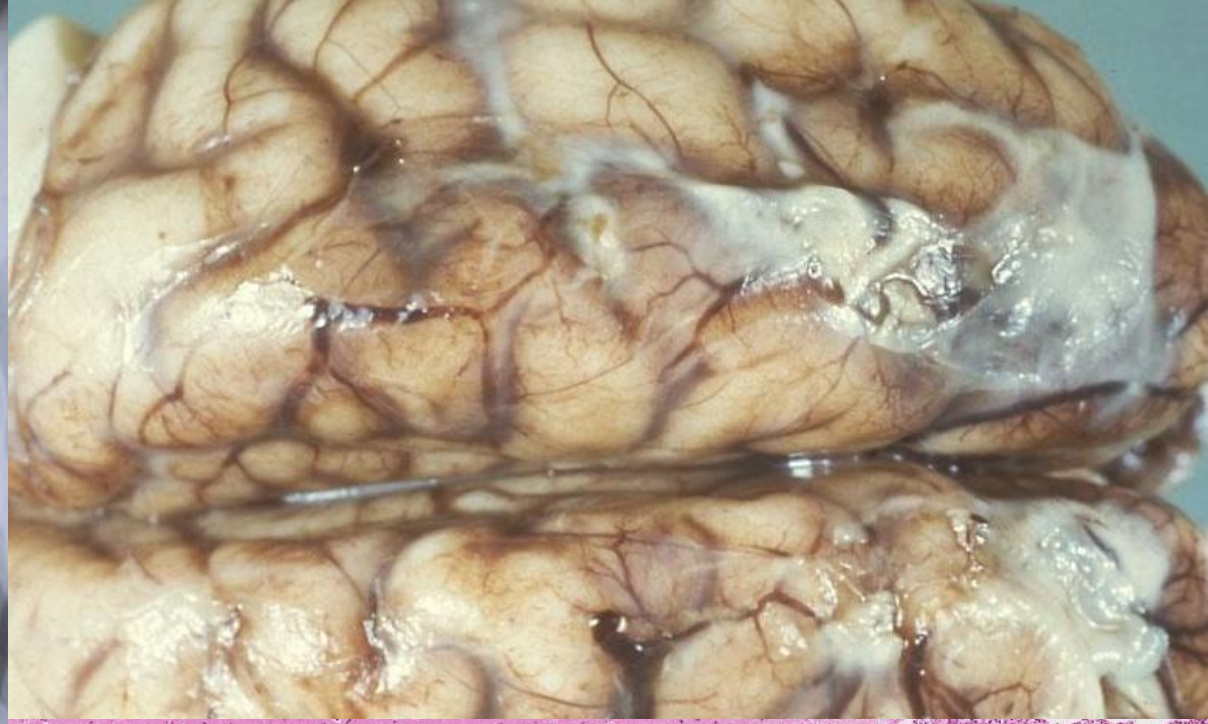
- The classic LOBAR pneumonia
- Normal flora in 20% of adults
- Only 20% of victims have + blood cultures
- "Penicillins" are often 100% curative
- Vaccines are often 100% preventive

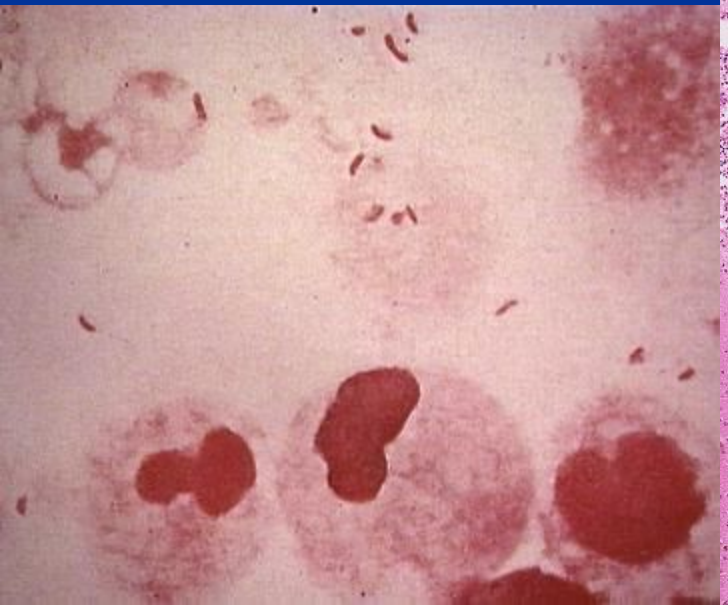


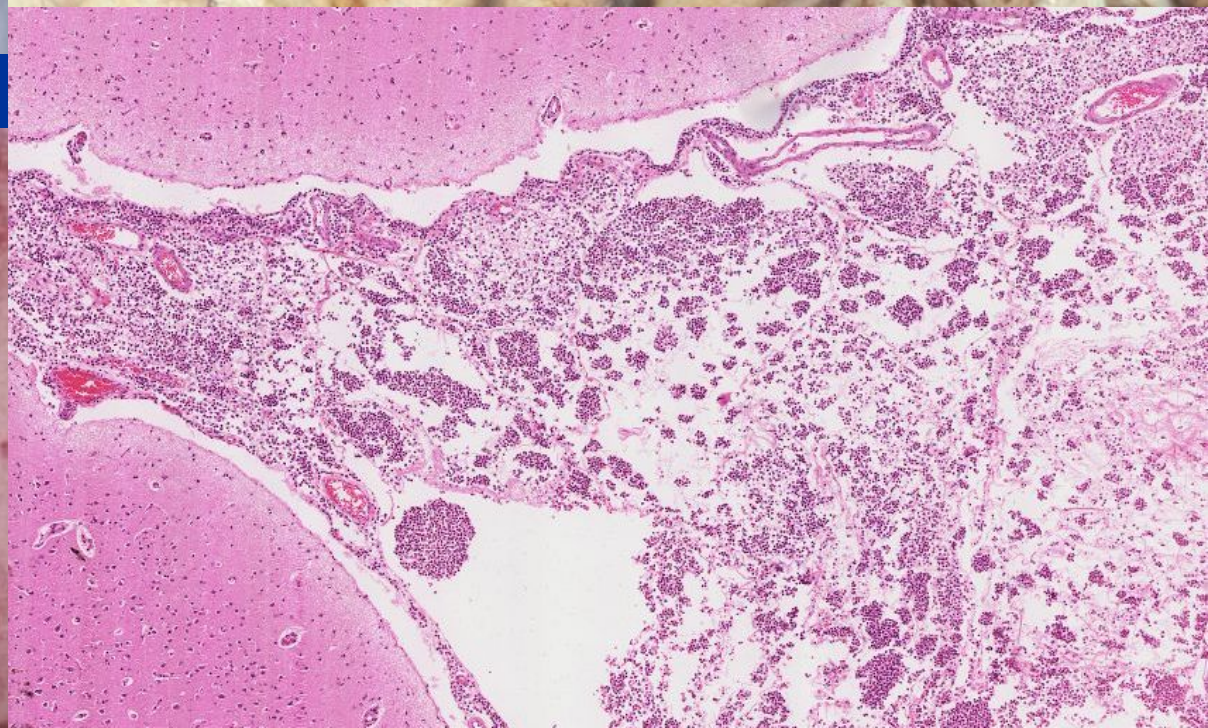












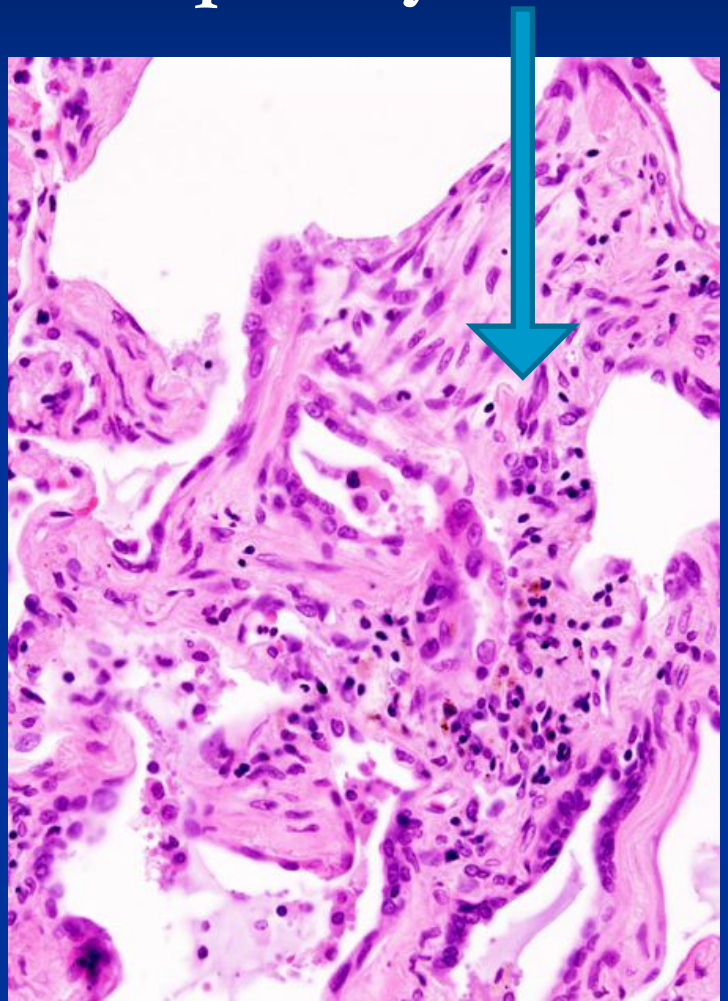
MORPHOLOGY

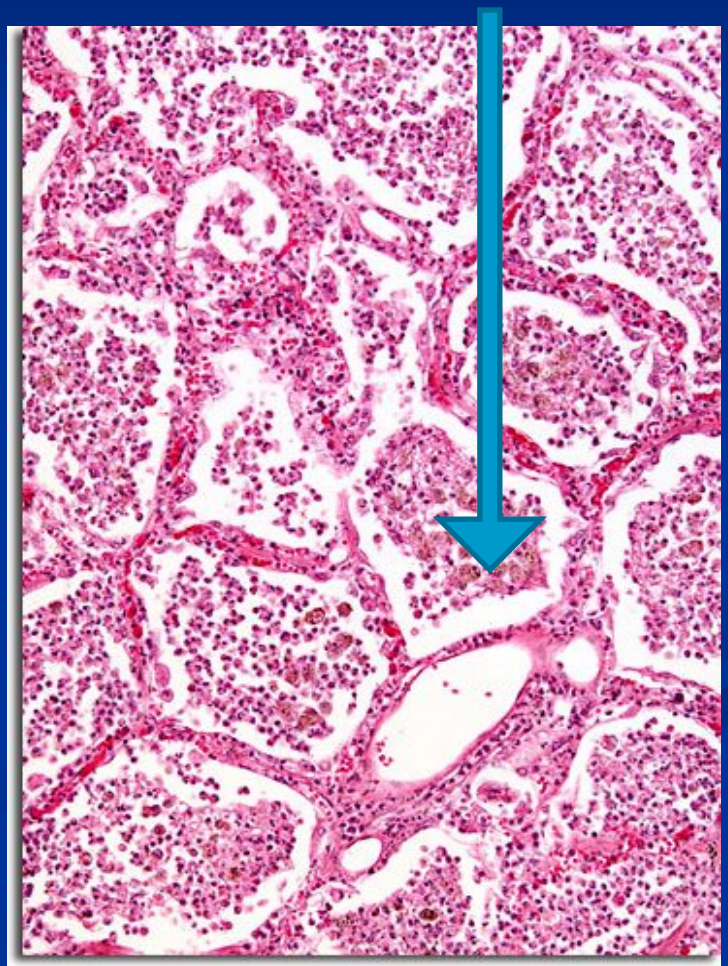
- ACUTE
- ORGANIZING
- CHRONIC
- FIBROSIS vs. FULL RESOLUTION

- "HEPATIZATION", RED vs. GREY
- CONSOLIDATION
- "INFILTRATE", XRAY vs. HISTOPATH
- Loss of "CREPITANCE"

VIRAL PNEUMONIAS

- Frequently “interstitial”, NOT alveolar





ASPIRATION PNEUMONIAS

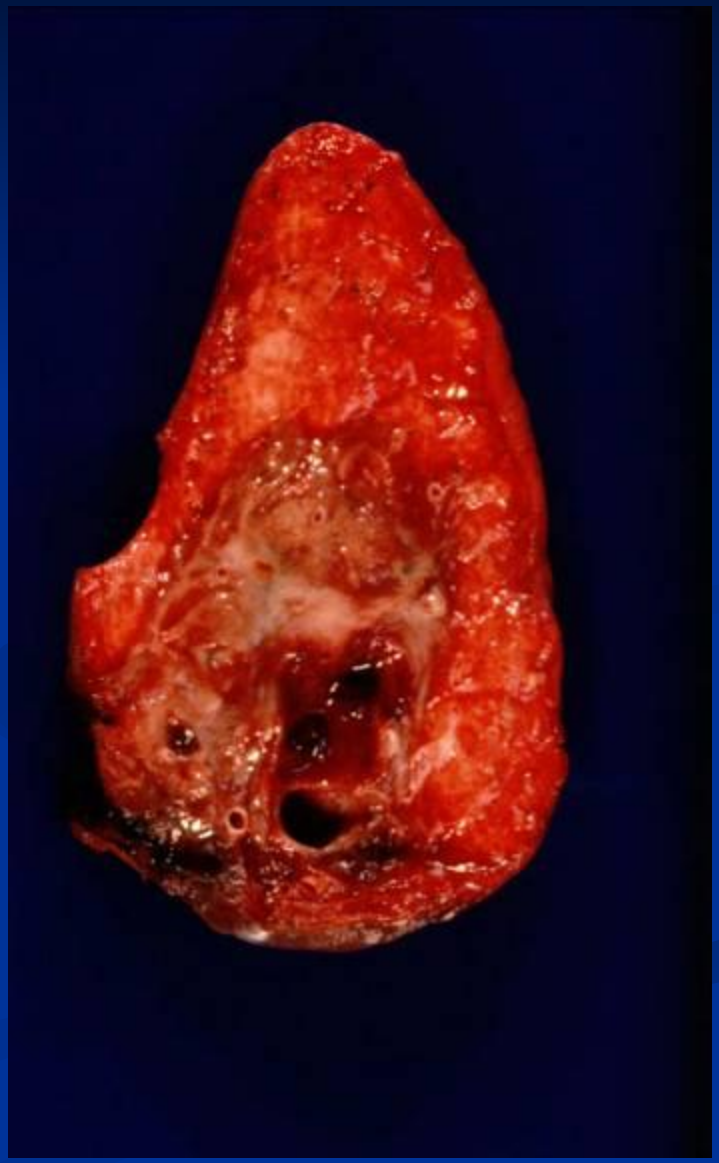
- UNCONSCIOUS PATIENTS
- PATIENTS IN PROLONGED BEDREST
- LACK OF ABILITY TO SWALLOW OR GAG
- USUALLY CAUSED BY ASPIRATION OF GASTRIC CONTENTS
- POSTERIOR LOBES (gravity dependent) MOST COMMONLY INVOLVED, ESPECIALLY THE SUPERIOR SEGMENTS of the LOWER LOBES
- Often lead to ABSCESSES

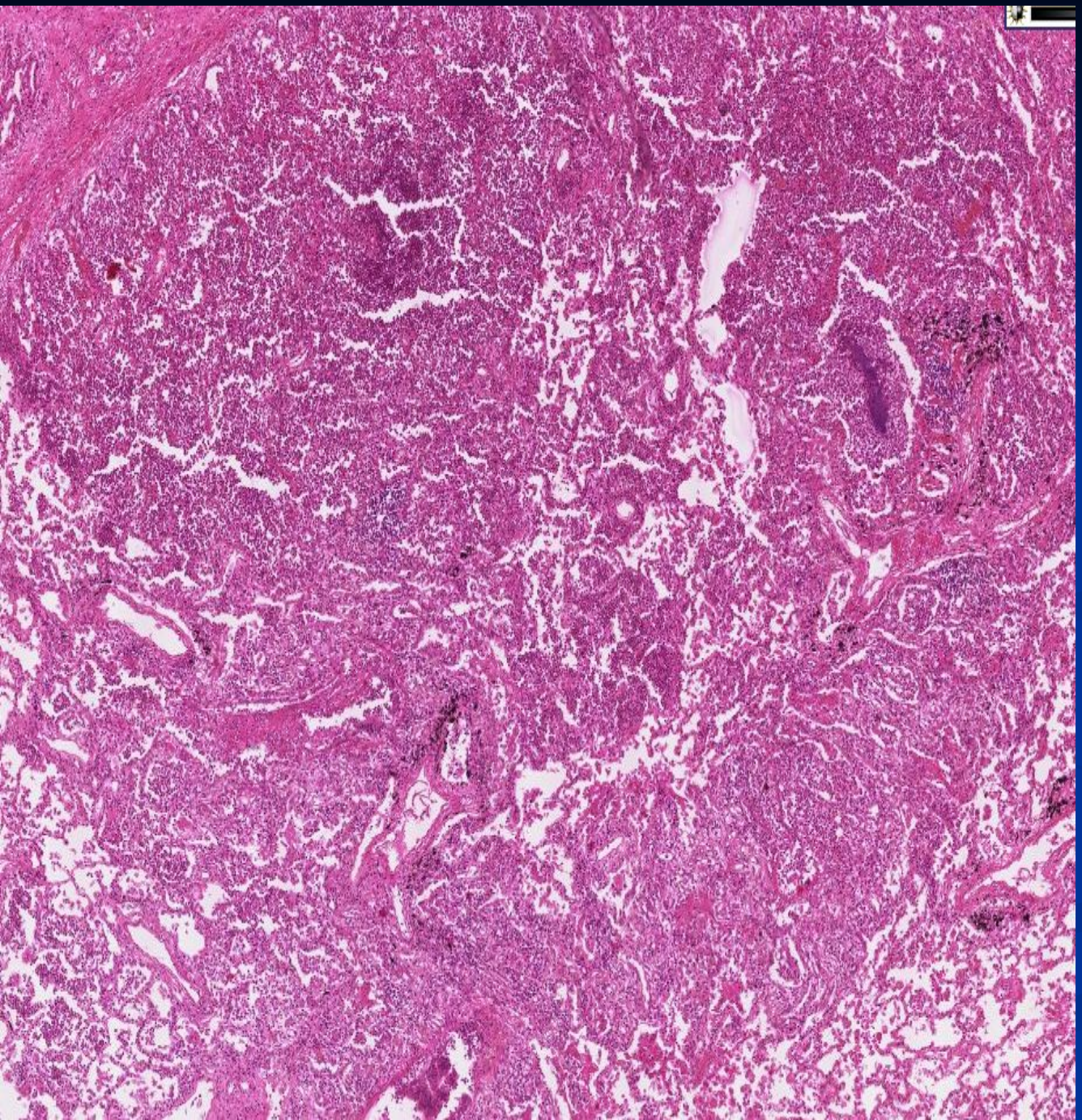
LUNG ABSCESSES

- ASPIRATION
- SEPTIC EMBOLIZATION
- NEOPLASIA
- From NEIGHBORING structures:
  - ESOPHAGUS
  - SPINE
  - PLEURA
  - DIAPHRAGM
- ANY pneumonia which is severe and destructive, and UN-treated enough

Lung abscess

- Localized suppurative necrosis
- Organisms commonly cultured:
  - Staphylococci
  - Streptococci
  - Gram-negative
  - Anaerobes
  - Frequent mixed infections
- Pathogenesis:
  - Aspiration
  - Pneumonia
  - Septic emboli
  - Tumors
  - Direct infection





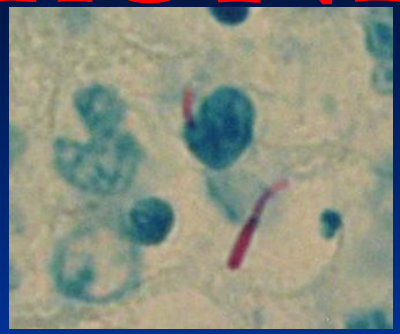
An abscess can be thought of as a pneumonia in which all of the normal lung outline can no longer be seen, and there is 100% pus.

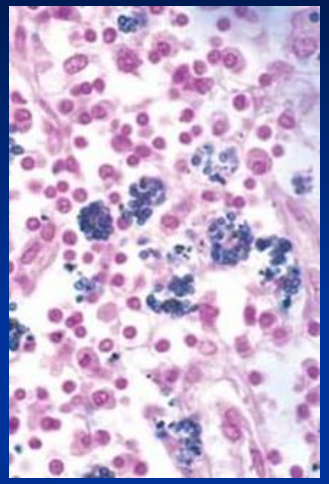
CHRONIC Pneumonias

- USUALLY NOT persistences of the community or nosocomial bacterial infections, but CAN BE, at least histologically
- Often SYNONYMOUS with the 4 classic fungal or granulomatous pulmonary infections infections, i.e., TB, Histo-, Blasto-, Coccidio-
- If you see pulmonary granulomas, think of a CHRONIC process, often years

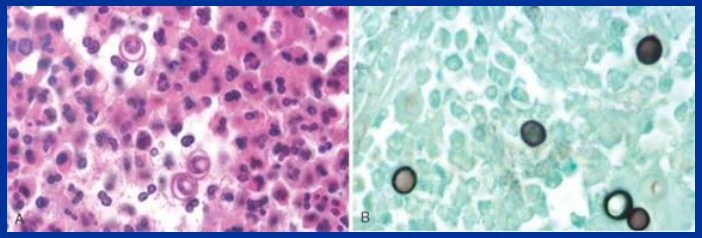
CHRONIC Pneumonias

- TB

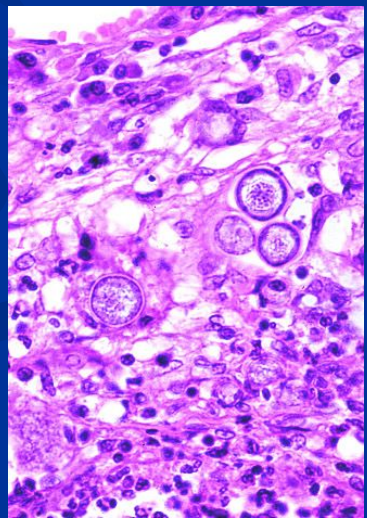


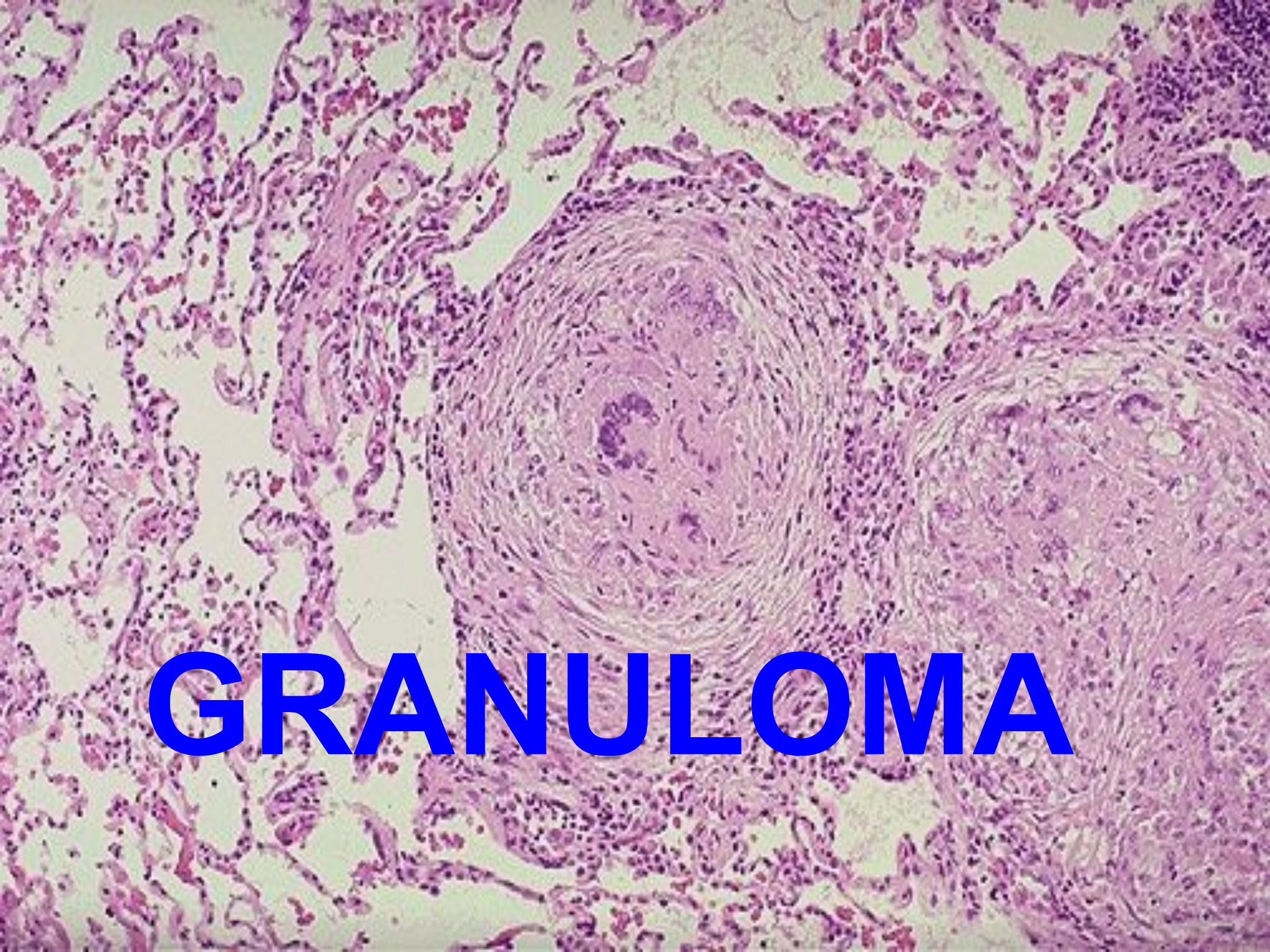


- HISTO-PLASMOSIS
- BLASTO-MYCOSIS



- COCCIDIO-MYCOSIS




GRANULOMA

LUNG TUMORS

- Benign, malignant, epithelial, mesenchymal, but 90% are CARCINOMAS
- BIGGEST USA killer. Why? Ans: Prevalence not as high as prostate or breast but mortality higher. Only 15% 5 year survival.
- TOBACCO has polycyclic aromatic hydrocarbons, such as benzopyrene, anthracenes, radioactive isotopes
- Radiation, asbestos, radon
- C-MYC, K-RAS, EGFR, HER-2/neu

PATHOGENESIS

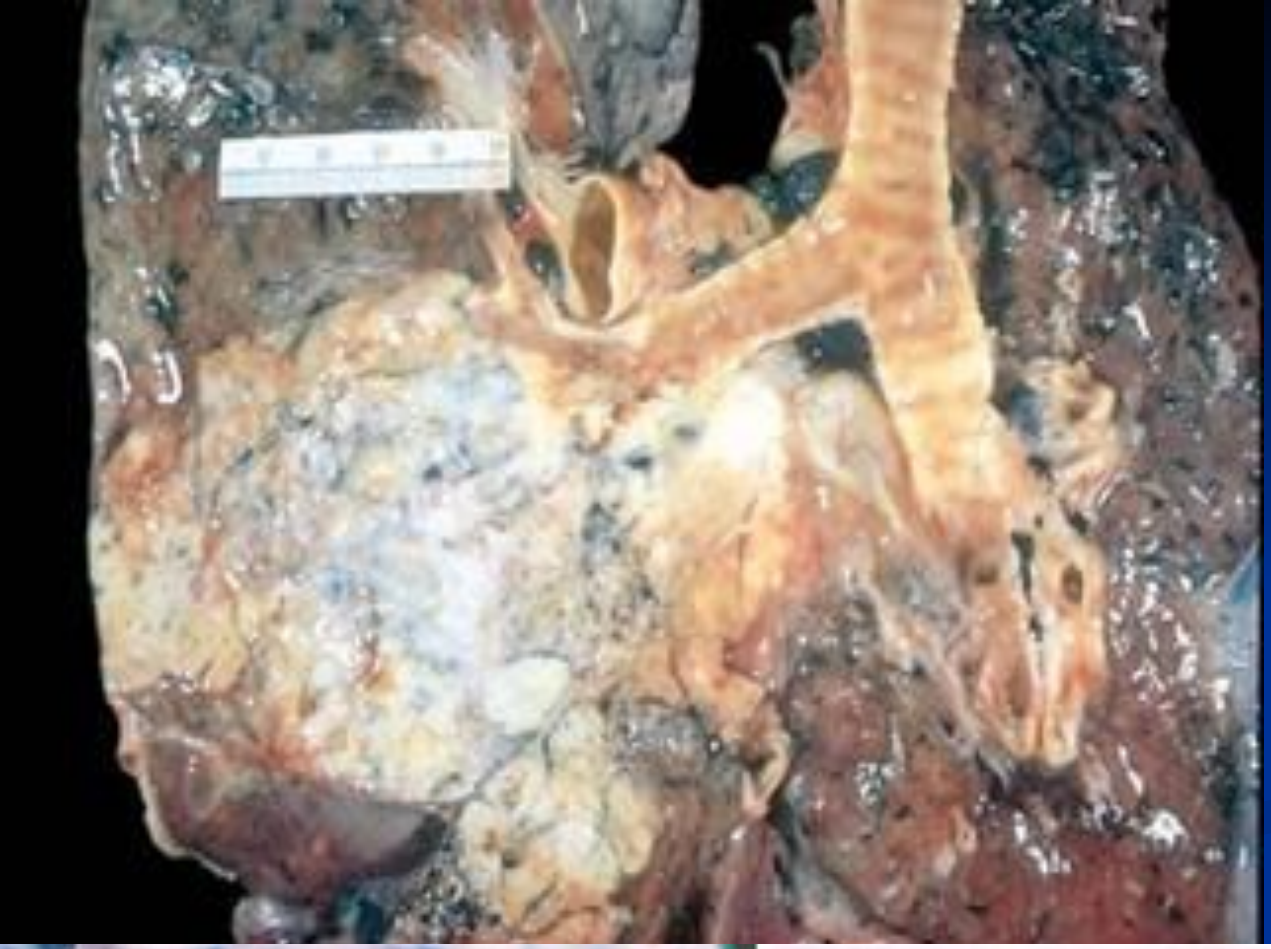
- NORMAL BRONCHIAL MUCOSA
- METAPLASTIC/DYSPLASTIC MUCOSA
- CARCINOMA-IN-SITU (squamous, adeno)
- INFILTRATING (i.e., “INVASIVE”) cancer

TWO TYPES

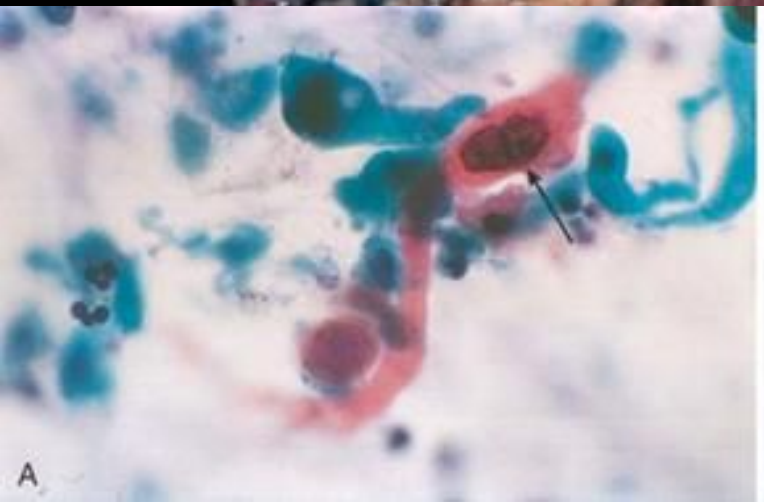
- NON-SMALL CELL
  - SQUAMOUS CELL CARCINOMA
  - ADENOCARCINOMA
  - LARGE CELL CARCINOMA
- SMALL CELL CARCINOMA

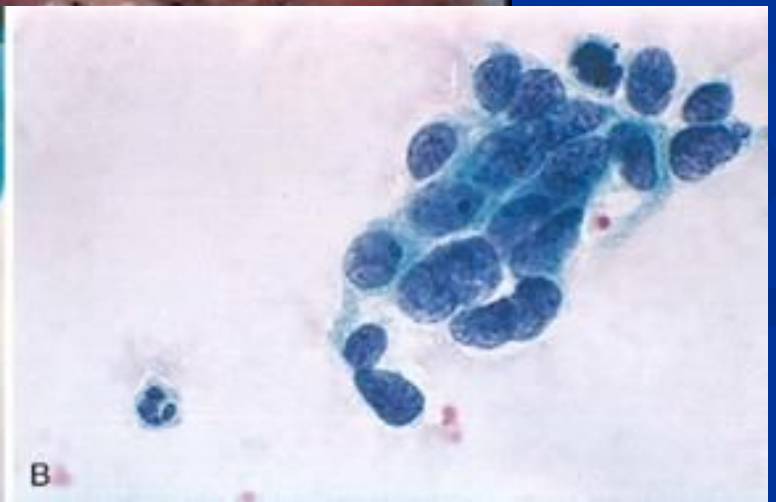
The BIG list

- Squamous cell carcinoma
- Small cell carcinoma
- Combined small cell carcinoma
- Adenocarcinoma: Acinar, papillary, bronchioloalveolar, solid, mixed subtypes
- Large cell carcinoma
- Large cell neuroendocrine carcinoma
- Adenosquamous carcinoma
- Carcinomas with pleomorphic, sarcomatoid, or sarcomatous elements
- Carcinoid tumor: Typical, atypical
- Carcinomas of salivary gland type
- Unclassified carcinoma



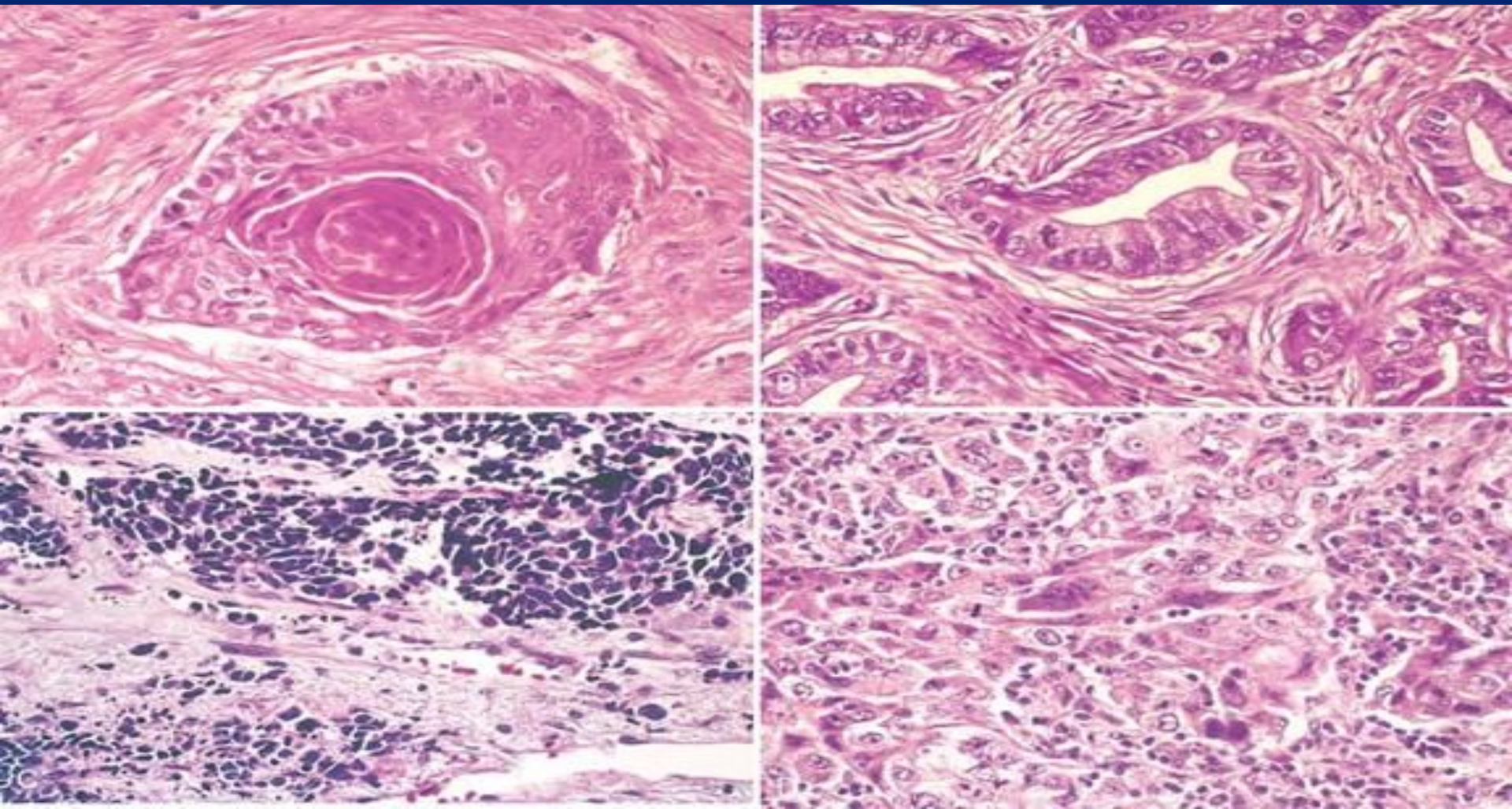
The classical squamous cell carcinoma starting in a large bronchus centrally, with bronchial obstruction. Adenocarcinomas tend to be more peripheral. Note the features of malignant cells on sputum cytology.





Name the four most common histologic patterns of lung carcinoma and explain why!

Squamous, adeno, large, small.



LOCAL effects of LUNG CANCER

Clinical Feature	Pathologic Basis
Pneumonia, abscess, lobar collapse	Tumor obstruction of airway
Lipid pneumonia	Tumor obstruction; accumulation of cellular lipid in foamy macrophages
Pleural effusion	Tumor spread into pleura
Hoarseness	Recurrent laryngeal nerve invasion
Dysphagia	Esophageal invasion
Diaphragm paralysis	Phrenic nerve invasion
Rib destruction	Chest wall invasion
SVC syndrome	SVC compression by tumor
Horner syndrome	Sympathetic ganglia invasion
Pericarditis, tamponade	Pericardial involvement

SVC, superior vena cava.

METASTATIC TUMORS

- LUNG is the MOST COMMON site for all metastatic tumors, regardless of site of origin
- It is the site of FIRST CHOICE for metastatic sarcomas for purely anatomic reasons!

PLEURA

- PLEURITIS
- PNEUMOTHORAX
- EFFUSIONS
  - HYDROTHORAX
  - HEMOTHORAX
  - CHYLOTHORAX
- MESOTHELIOMAS

PLEURITIS

- Usual bacteria, viruses, etc.
- Infarcts
- Lung abscesses, empyema
- TB
- "Collagen" diseases, e.g., RA, SLE
- Uremia
- Metastatic

PNEUMOTHORAX

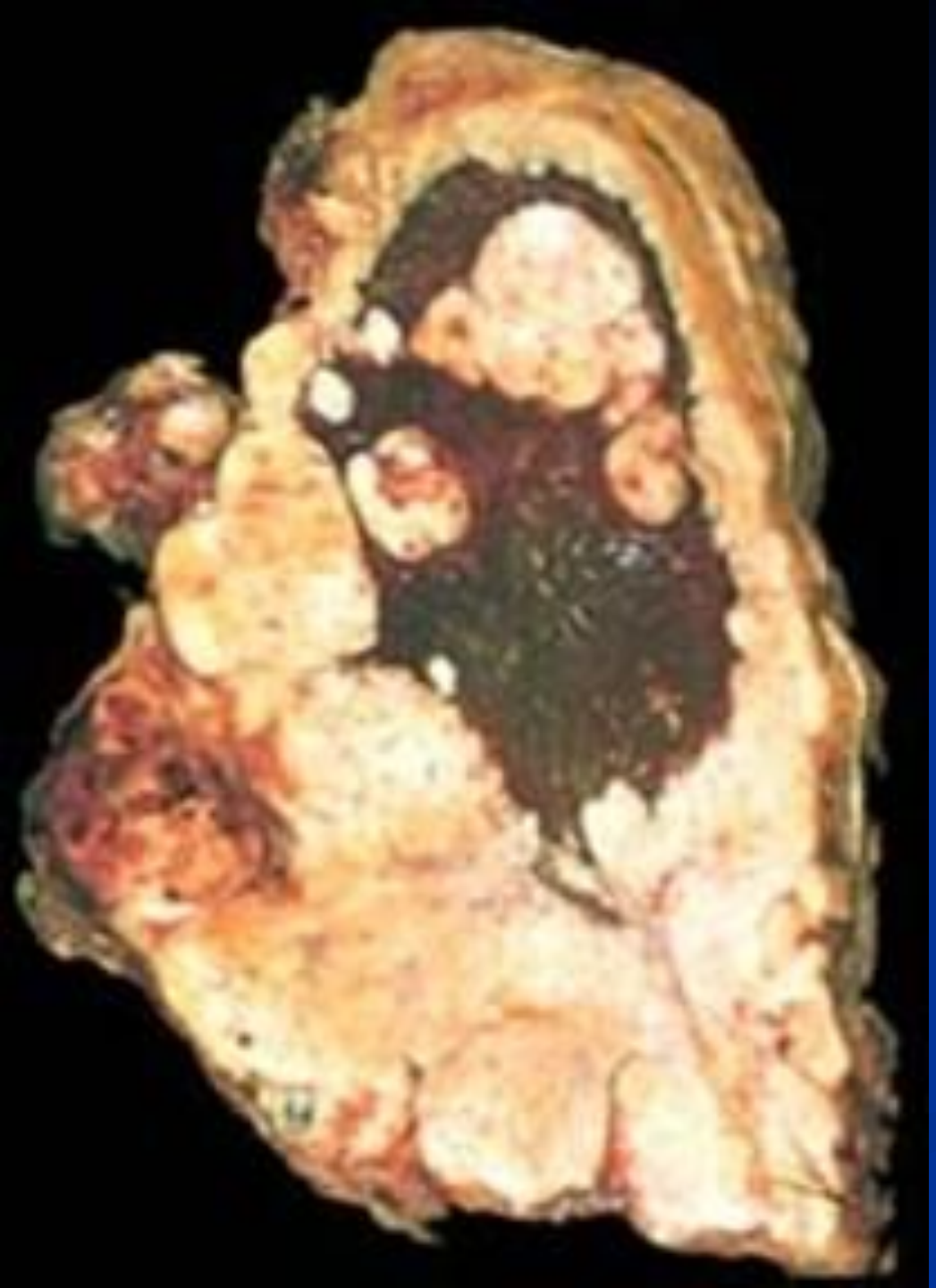
- SPONTANEOUS, TRAUMATIC, THERAPEUTIC
- OPEN or CLOSED
- "TENSION" pneumothorax, "valvular" effect
- "Bleb" rupture
- Perforating injuries
- Post needle biopsy

EFFUSIONS

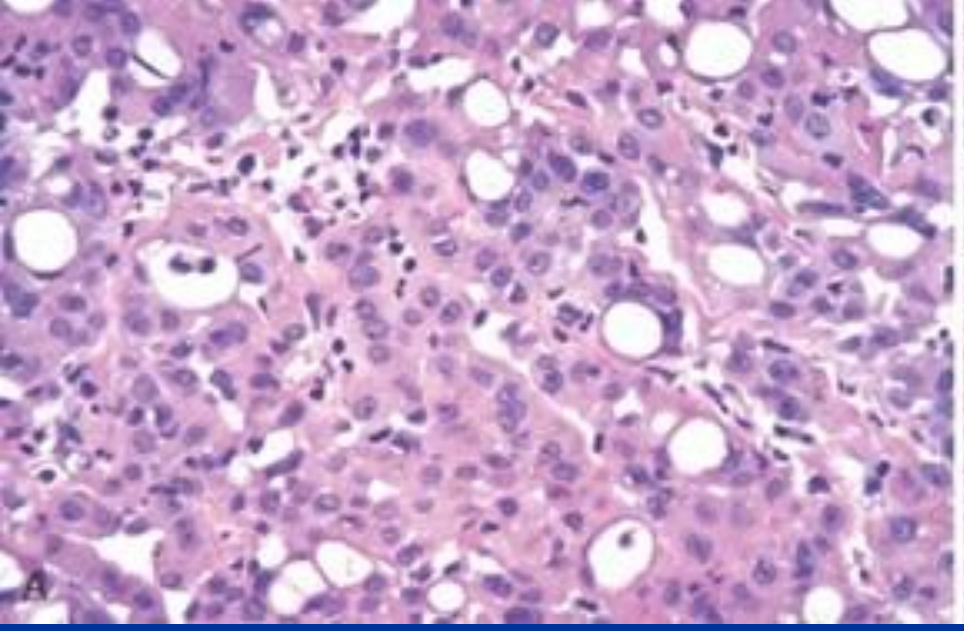
- TRANSUDATE (HYDROTHORAX)
- EXUDATE (HYDROTHORAX)
- BLOOD (HEMOTHORAX)
- LYMPH (CHYLOTHORAX)

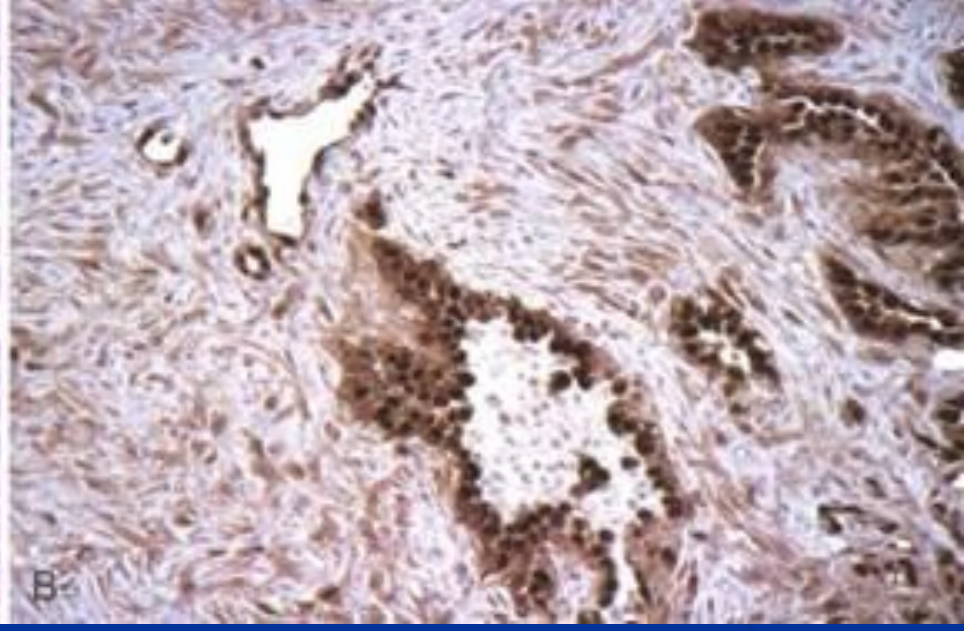
MESOTHELIOMAS

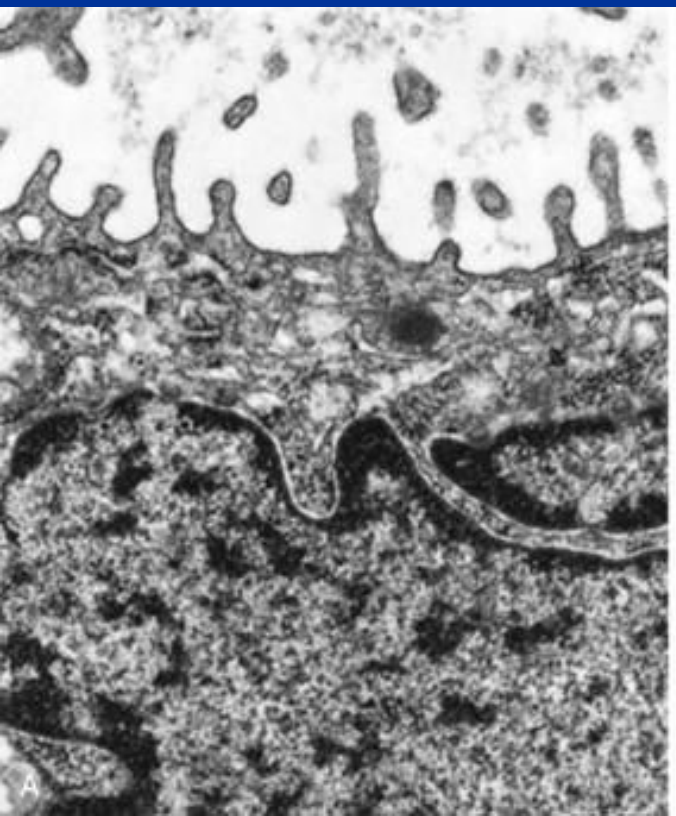
- "Benign" vs. "Malignant" differentiation does not matter, but a self limited localized nodule can be regarded as benign, and a spreading tumor can be regarded as malignant
- Visceral or parietal pleura, pericardium, or peritoneum
- Most are regarded as asbestos caused or asbestos "related"

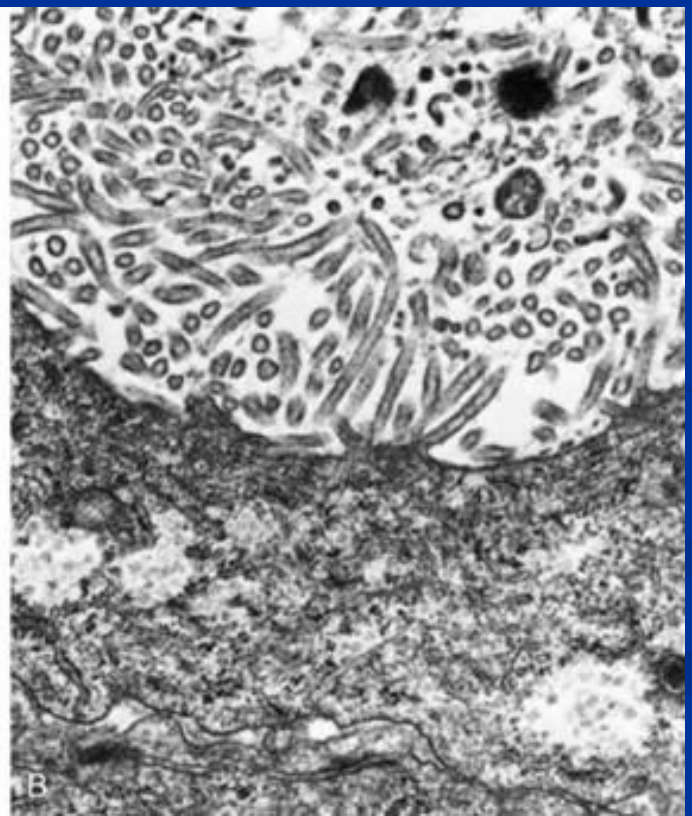


Typical growth appearance of a malignant mesothelioma, it compresses the lung from the OUTSIDE.









H&E, IMMUNOCHEMISTRY

- **EM**