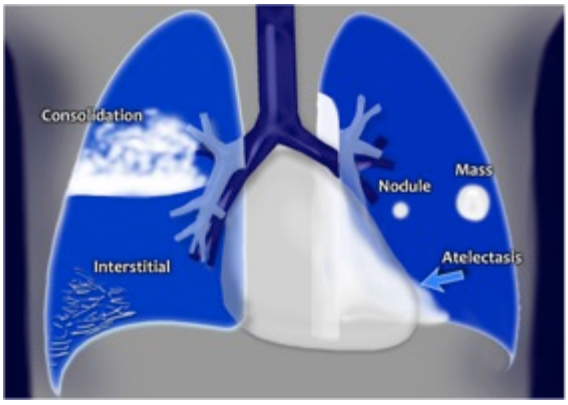
Sources: Prof notes + my notes, DR. JALAN'S LUNG PATH NOTES,, past tutoring slides, dabbles of about 239048 websites, http://radiopaedia.org

PATHOLOGY II

RESPIRATORY PATHOLOGY



CHEST X-RAY (CXR) PATTERNS

1. CONSOLIDATION: fills the alveoli with fluid
2. INTERSTITIAL: supporting tissue showing fine or coarse reticular opacities or small nodules
3. NODULES or MASSES: space occupying lesion, either solitary or multiple
4. ATELECTASIS: collapse of a part of the lung
5. CAVITY: a gas-filled area in the center of a nodule or mass, typically thick-walled

4 ANATOMIC COMPARTMENTS ASSOCIATED WITH DISEASE

- AIRWAYS
  - Chronic Obstructive Pulmonary Disease (COPD) + 5 Types, Asthma
- INTERSTITIUM
  - **Fibrosing** – Pneumoconiosis (Coal Workers, Silicosis), Asbestosis, Drug/Radiation ILD, Usual Interstitial Pneumonia (UIP/IPF), Nonspecific Interstitial Pneumonia (NSIP), Cryptogenic Organizing Pneumonia (COP)/Bronchiolitis Obliterans
  - **Granulomatous** – Hypersensitivity Pneumonitis (Extrinsic Allergic Alveolitis), Sarcoidosis, Tuberculosis
  - **Eosinophilic**
  - **Smoking-Related** –Respiratory Bronchiolitis-Associated ILD (RB-ILD), Desquamative Interstitial Pneumonia (DIP)
- BLOOD VESSELS – Pulmonary HTN, Emboli
- ALVEOLI – Pneumonia, Edema

LOWER LOBE/BIBASILAR: BAD RASH

B – Bronchiectasis
A – Aspiration
D – Desquamative Interstitial Pneumonia (DIP)

R – Rheumatoid Arthritis
A – Asbestosis
S – Scleroderma
H – Hamman Rich (Acute Interstitial Pneumonia-AIP)

UPPER LOBE/APICAL: SET CAP

S – Sarcoidosis/Silicosis
E – EG/Extrinsic Allergic Alveolitis
T – TB/fungal

C – Cystic fibrosis
A – Ankylosing spondylitis
P – Pneumocytis pneumonia (PCP)

PERIPHERAL OPACITIES: SIC CUE

S – Sarcoidosis
I – Infarction
C – Cryptogenic Organizing Pneumonia (COP)

C – Contusion
U – Usual Interstitial Pneumonia (UIP)/
Desquamative Interstitial Pneumonia (DIP)
E – Eosinophilic pneumonia

PULMONARY CAVITY: Gas filled areas in center of nodule/mass

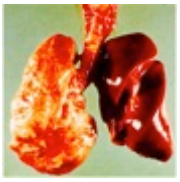
C – Cancer (SCC most common)
A – Autoimmune (Wegener's granulomas, RA nodules)
V – Vascular (pulmonary embolism, infarction)
I – Infection (abscesses, TB)
T – Trauma
Y – Youth/Congenital (bronchogenic cyst, pulmonary sequestrations, bronchopulmonary malformation)

IDIOPATHIC ILD:

All **I**diopathic **C**hronic **L**ung **D**iseases a**R**e **N**onspecific

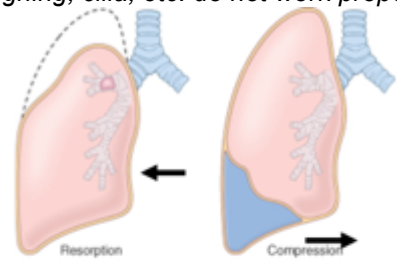
AIP IFP/UIP COP LIP DIP RB-ILD NSIP

ATELECTASIS: "Collapsed Lung"

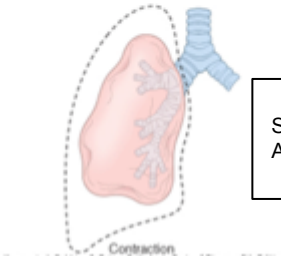


- *Incomplete expansion **(neonatal – image)** or the collapse of previously inflated lung **(adult)***
- Acquired collapse (**Adult)**
  - **Resorption (obstruction), Compression, Contraction**
- All atelectasis at risk for infection
  - Predilection for the development of **bronchopneumonia** – *No removal of trapped bacteria in the collapsed lung because coughing, cilia, etc. do not work properly*

RESORPTION
Lung shifts to fill empty void & heart swings with it – shifts TOWARD collapsed lung



COMPRESSION
AIR/FLUID in pleural space
Increased pressure pushes heart & mediastinum AWAY from collapsed lung
**tension pneumothorax*



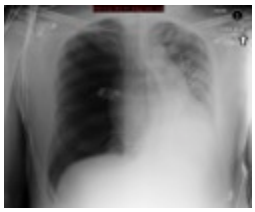
CONTRACTION
SCARRING of the lung prevents full expansion
Associated with Restrictive Lung Disease
**pulmonary fibrosis*

1. RESORPTIVE ATELECTASIS

- Complete airway obstruction with subsequent absorption of trapped air
- Most often the result of mucus plugs or exudates within the lumen
  - ***Often due to chronic bronchitis, asthma, bronchiectasis***
- Other causes: aspiration of foreign bodies, large extrinsic masses, intramural & luminal masses
- **MEDIASTINAL SHIFT TOWARD COLLAPSED LUNG**

2. COMPRESSION ATELECTASIS

- Compression of lung from pressure generated in outside space
- Results from excessive accumulation of fluid, blood, or air within the pleural cavity or from large tumor mass pressure on the lung
  - *Fluid accumulating in pleural cavity is most commonly encountered in patients with cardiac failure & neoplastic infiltration*
- **MEDIASTINAL SHIFT AWAY FROM AFFECTED LUNG**
- **TENSION PNEUMOTHORAX**: air can enter but cannot escape ("ball valve"), resulting in increased pleural pressure; forces mediastinum AWAY

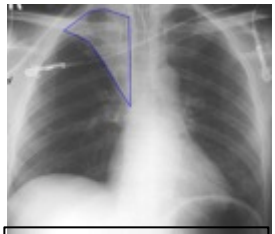


R SIDED TENSION PNEUMOTHORAX –
Notice mediastinal shift to the left

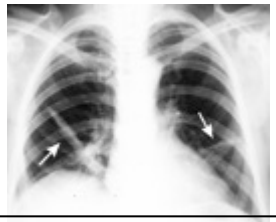
- **SPONTANEOUS PNEUMOTHORAX:** due to rupture of small bleb of the lung; NO SHIFT in the mediastinum; will present with sudden onset CP, usually male

3. CONTRACTION ATELECTASIS

- Occurs in regions of pulmonary fibrosis (Restrictive Lung Disease) – *prevents full expansion*
- The only **irreversible** form of atelectasis – *It's essentially scarring of the lung*



RUL ATELECTASIS



LINEAR ATELECTASIS

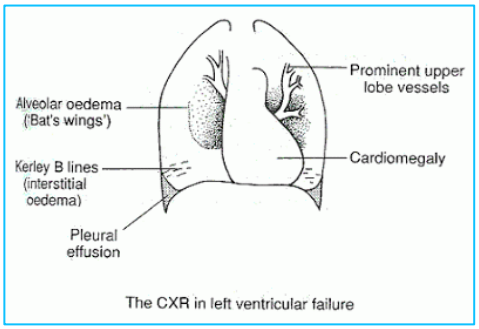
PULMONARY EDEMA

- Leakage of excessive interstitial fluid with accumulation in alveolar spaces

CLINICAL FEATURES

- Dyspnea (rapid, shallow breathing), orthopnea (dyspnea worsens w/ lying flat), paroxysmal nocturnal dyspnea, cough (+/- ***pink frothy sputum-surfactant***)
- Rales on auscultation
- **CXR**: **Kerley B lines/Butterfly pattern**

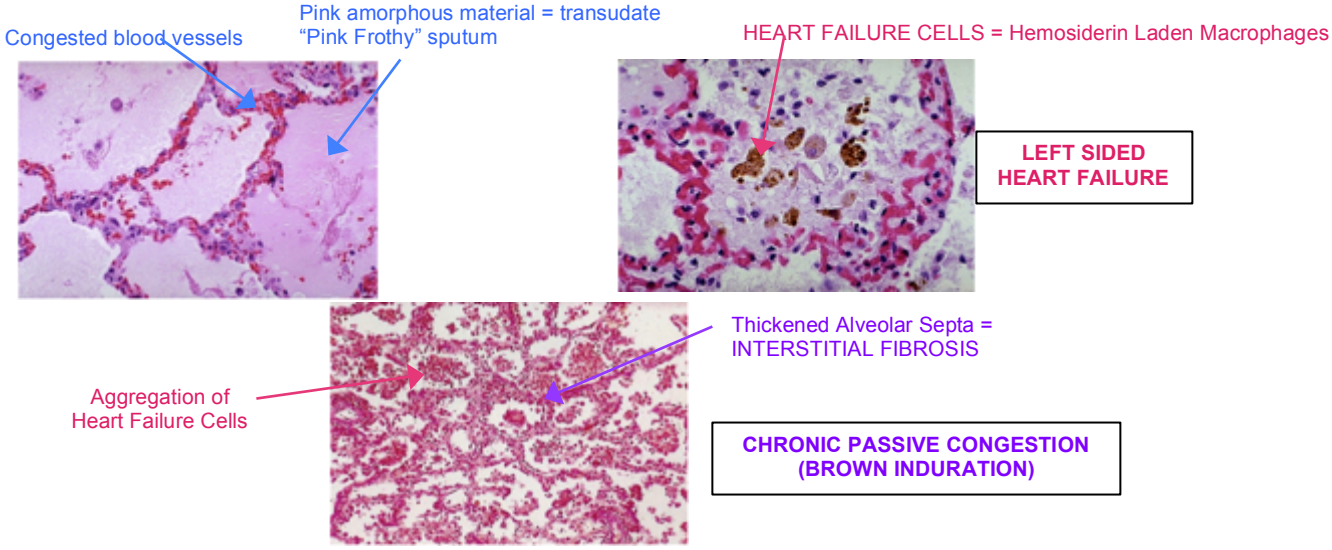
MNEMONIC FOR CXR
A – Alveolar Edema (Bat Wings/Butterfly)
B – B Kerley **B** lines (Interstitial Edema)
C – Cardiomegaly
D – Dilated prominent upper lobe vessels
E – E Pleural **E**ffusion



The CXR in left ventricular failure

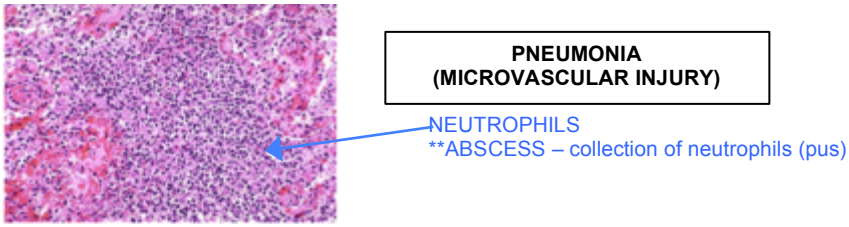
1. HEMODYNAMIC DISTURBANCES – Most Common Cause!

- **CAUSES**:
  - Increased pulmonary venous pressure – more fluid driven out of circulation into interstitium
    - *Left sided heart failure, volume overload*
  - Decreased oncotic pressure – water moves towards higher protein concentratin
    - *Hypoalbuminemia, nephrotic syndrome, liver disease*
  - Lymphatic obstruction
- BASAL **LOWER LOBES**
- **"Heart failure cells" = Hemosiderin laden macrophages**
- If chronic, leads to **alveolar fibrosis (brown induration of lung)**

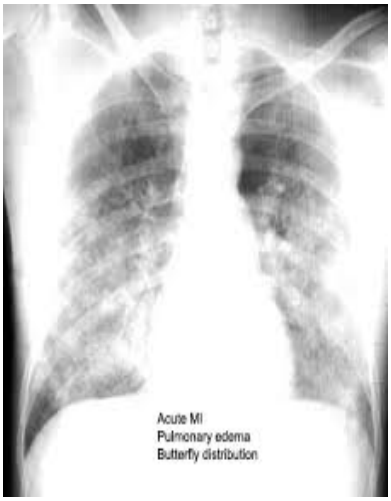


2. MICROVASCULAR (ALVEOLAR) INJURY → INCREASED CAPILLARY PERMEABILITY

- Injury to capillaries of the alveolar septa
- CAUSES:
  - Direct injury – *bacterial infection, inhaled gases*
    - **Acute Endocarditis** caused by *STAPH aureus* infection – damage to previously HEALTHY valves, vegetations can break off causing SEPTIC EMBOLI (can infect brain); typically seen in IV drug users who shoot up in veins, thus affecting right side of heart first
    - **Subacute Endocarditis** caused by *STREP viridans* infection – damage to previously DAMAGED valves
  - Indirect injury – *septicemia, blood transfusion, shock*
- If diffuse alveolar damage → **Acute Respiratory Distress Syndrome (ARDS)**



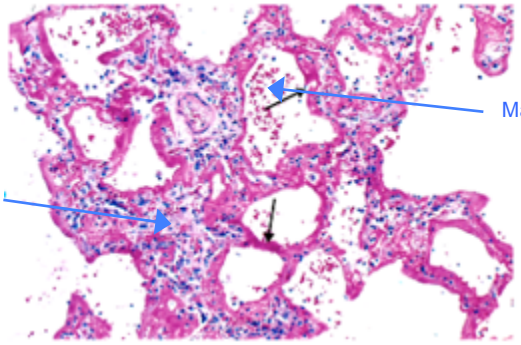
INTERSTITIAL EDEMA by edema in intra-lobular septum
***Note Kerley B lines*



ACUTE MI W/ LEFT VENTRICULAR WALL DYSFUNCTION causes increased pressure in the pulmonary venous system, which backs up into the pulmonary capillary system inducing **pulmonary edema**. Diuretics are used to decreased intravascular volume in an effort to decrease intravascular pulmonary capillary pressure.
***Note butterfly pattern*

ACUTE RESPIRATORY DISTRESS SYNDROME (ARDS) – *Also more on this later...*

- Diffuse alveolar damage characterized by leaky pulmonary capillaries – *fibrin leaks out, lining alveolar spaces → decreased gas exchange*
- Generally a complication of the following conditions:
  - Shock, secondary to sepsis – *gram negative bacteria: toxins travel in blood to lung causing pulmonary capillary damage*
  - Trauma
  - Acute hemorrhagic pancreatic necrosis (pancreatitis)
  - Burns
  - Complicated abdominal surgery
- Rapid onset of severe life-threatening respiratory insufficiency
- Tachycardia & cyanosis – response to hypoxemia
  - Severe hypoxemia is refractory to oxygen therapy



Black Arrows = Fibrin lining the alveolar spaces – blocking gas exchange

CONGENITAL (DEVELOPMENTAL) ANOMALIES

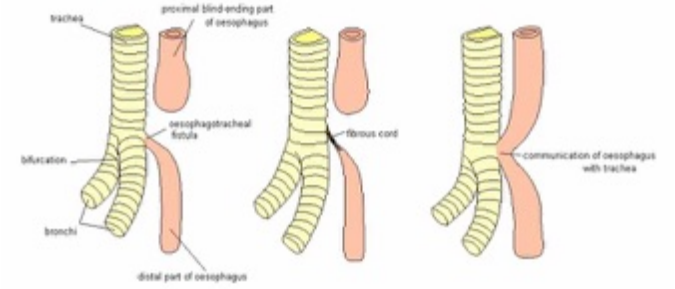
- **Agenesis**: failure of an organ (i.e. lungs) to develop during embryonic growth
- **Hypoplasia**: underdevelopment of an organ
- Tracheal and/or bronchial abnormalities: Atresia, Stenosis, Tracheoesophageal Fistula
- Congenital Foregut Cysts: Bronchogenic, Esophageal, Enteric – *lungs arise from ventral wall foregut*
- Sequestrations of lung tissue

PULMONARY HYPOPLASIA

- Underdevelopment of the lung
- Common (10% neonatal autopsy)
- Seen with fetal compression & with other anomalies

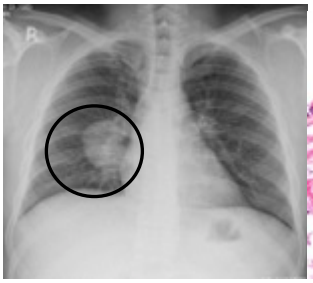
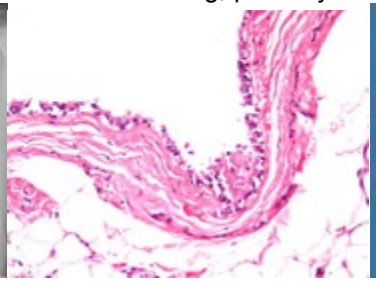
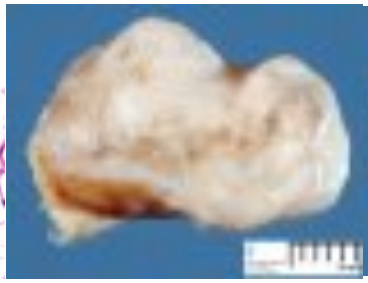
TRACHEOESOPHAGEAL FISTULA

- Connection between 2 openings
- *Air seen in the stomach & makes you think the baby can swallow properly, but the baby has trouble eating because the esophagus ends in blind pouch*



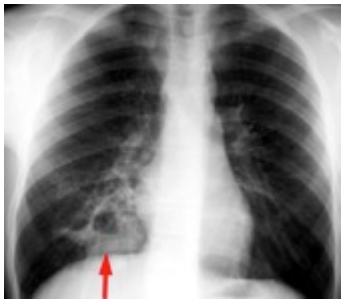
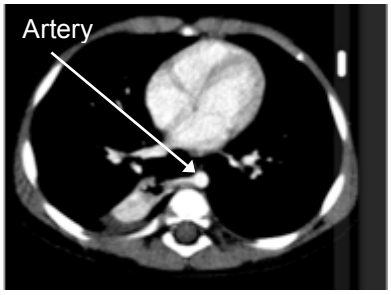
CONGENITAL FOREGUT CYSTS

- Detached section of mal-developed foregut
- **MEDIASTINAL** & **HILAR** locations
- Not connected to airways
- Usually bronchogenic with respiratory epithelium +/- cartilage +/- smooth muscle & filled with mucin
- Presents as mass or incidental finding, possibly in adulthood


BRONCHOPULMONARY SEQUESTRATIONS

- Area of lung without normal connection to the airway system & abnormal blood supply arising from the aorta or its branches
- **EXTRALOBAR (15-25%):** found in thorax or mediastinum external to lung; diagnosed as mass lesions & may have other congenital anomalies
- **INTRALOBAR (75-85%):** found in the lung; have **recurrent infections** in the sequestration or bronchiectasis; most likely an acquired lesion, where bronchial connect is lost & vascular pattern changes

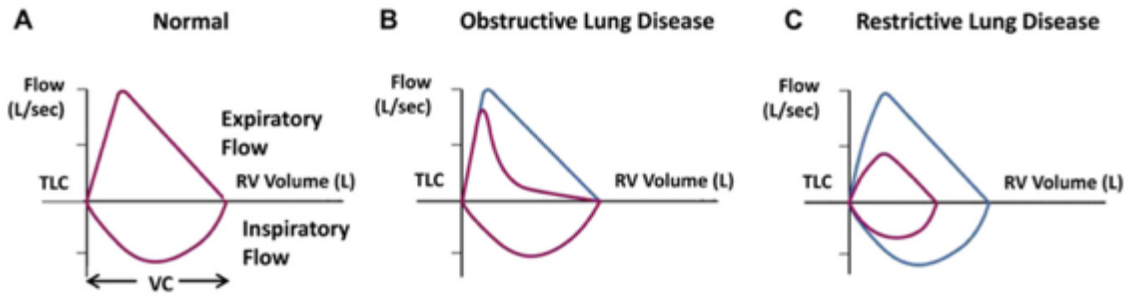
CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

RESTRICTIVE LUNG DISEASE

- Reduced expansion of the lung parenchyma (interstitium) & decreased TLC
- **Reduced chest wall expansion**
- *Reduced ability to ventilate due to fibrosing lung disease*
- Near normal flow rates (FEV1 may be mildly reduced due to decreased TLC)
- *Interstitial fibrosis, pneumoconiosis, ARDS, chest wall disorders (kyphosis), & obesity*

OBSTRUCTIVE LUNG DISEASE

- **Increased airway resistance due to partial or complete obstruction**
- *Reduced ability to ventilate due to airway restriction or loss of elastic recoil*
- Limited rate of flow
- FEV1/FVC reduced at <70%



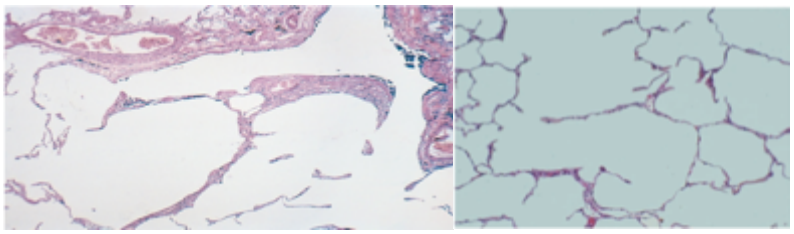
Measure	Obstruction	Restriction	Mixed
FEV1/FVC	Decreased	Normal or increased	Decreased
FEV1	Decreased	Decreased, normal or increased	Decreased
FVC	Decreased or normal	Decreased	Decreased or normal
TLC	Normal or increased	Decreased	Decreased, normal or increased
RV	Normal or increased	Decreased	Decreased, normal or increased

FEV1 – Forced expiratory volume in 1 sec; FVC – Forced Vital Capacity; RV – Residual volume; TLC – Total lung capacity

TYPE OF COPD	ANATOMIC SITE	ETIOLOGY	PATHOLOGICAL CHANGES	SIGNS/SYMPTOMS
EMPHYSEMA	Acinus	**SMOKING**	Airspace enlargement Wall destruction	Dyspnea "PINK PUFFER"
CHRONIC BRONCHITIS	Bronchus	**SMOKING**, Pollutants	Mucus gland hyperplasia Mucus hyper-secretion Inflammation	Cough + sputum "BLUE BLOATER"
ASTHMA	Bronchus	Immunological	Smooth muscle hyperplasia Excessive mucus Inflammation	Episodic wheezing Cough Dyspnea
BRONCHIECTASIS	Bronchus	Persistent infection	Airway dilation & scarring	Cough + purulent sputum Fever

1. EMPHYSEMA – "Pink Puffer"

- Irreversible enlargement of airspaces DISTAL TO TERMINAL BRONCHIOLE *(respiratory bronchiole, alveolar ducts, & alveoli)* with alveolar destruction & **loss of elastic recoil**; *with no obvious fibrosis*
- No mass obstructing the airway, but the lack of elastin makes it hard for lungs to recoil

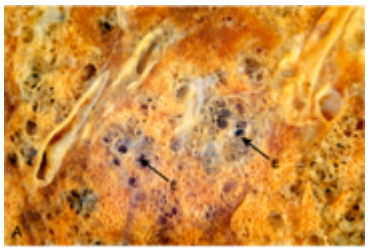


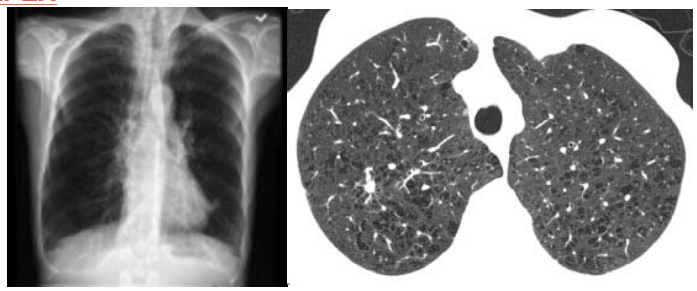
EMPHYSEMA
Disruption of the septa + **Increased air spaces**

CENTRIACINAR/CENTRILOBULAR EMPHYSEMA = SMOKERS!

- MOST COMMON (95%) of the clinically significant types of emphysema
- Occurs predominantly in HEAVY SMOKERS, *often associated with chronic bronchitis*
- Changes most notable in the **UPPER LOBES/APEX**

PATCHY DISTRIBUTION

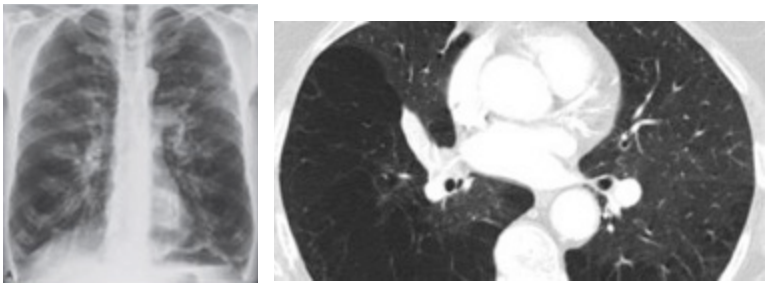




PANACINAR/PANLOBULAR EMPHYSEMA = α-1-ANTITRYPSIN DEFICIENCY!

- Destruction of the entire functional unit (ACINUS) from respiratory bronchiole to terminal blind alveoli
- Changes most notable in the **LOWER LOBES** & anterior margins of the lung
- Associated with α-1-antitrypsin deficiency
  - Enzyme made in the liver that normally degrades elastase
  - *With deficiency → proteolytic digestion of alveolar walls with neutrophils releasing elastase*
  - **Chromosome 14 (PiZZ)**
  - Emphysema + cirrhosis of the liver – *scarring due to build up of α-1-AT enzyme over time due to inability to transport enzyme*
- ***Made much worse with smoking!***

DIFFUSE DISTRIBUTION

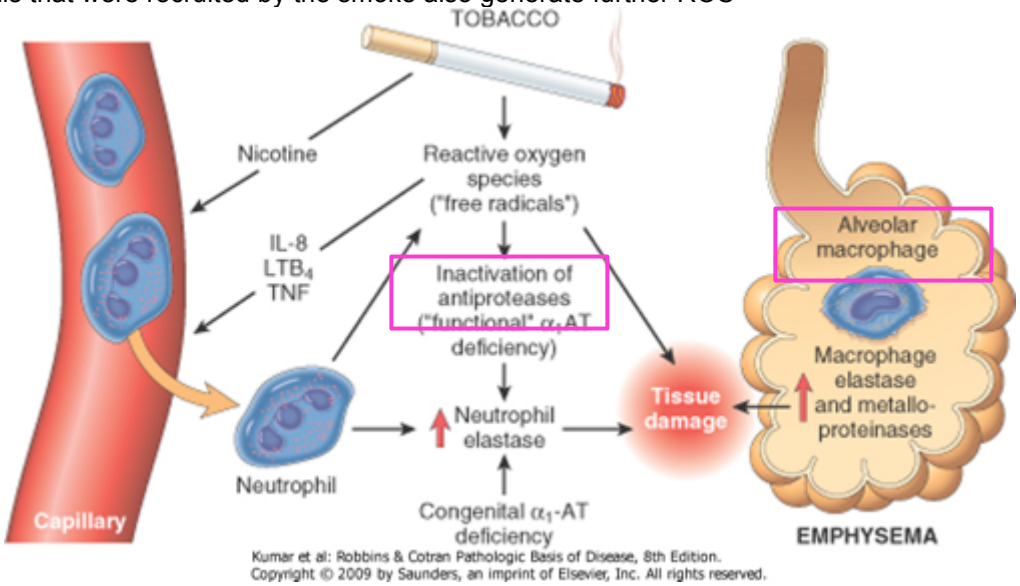


PARASEPTAL EMPHYSEMA

- Involves alveolar duct & alveoli, but spares the proximal respiratory bronchiole
- Predilection for the **UPPER LOBES** & along the pleura & margins of the lobule
- **Forms bullae** – large air filled spaces trapped below the pleura
- Blebs represent spaces between layers of the pleura & are responsible for most cases of **SPONTANEOUS PNEUMOTHORAX –** *Young male with sudden onset of chest pain & dyspnea; CXR will show subtle small amounts of air in the pleural space (thoracentesis results in rush of air)*

PATHOGENESIS OF EMPHYSEMA

- Smoke leads to production of chemotactic factors (IL-8, LTb4, TNF) + nicotine is itself chemotactic for neutrophils, which leads to increased secretion of elastase
- Smoke also releases ROS, which inactivate any functional α-1-antitrypsin in the area + increased elastase
- Neutrophils that were recruited by the smoke also generate further ROS

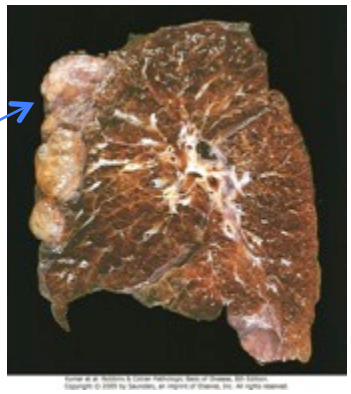


EMPHYSEMA – Clinical Manifestations

- Usually in **OLDER patients 50-70**
- Appears after at least 1/3 of the functional **parenchyma** has been incapacitated
- First manifestation: usually dyspnea +/- cough
  - HYPER-RESONANT when percussing the lung
- Increased weight loss – *constant feeling of not being able to breath, so don't eat as much*
- **BARREL-CHESTED** (increased AP diameter)
- Prolonged expiration
- **CHEST X-RAY** – Not diagnostic
  - Lung **HYPER-INFLATION** manifested as a flat diaphragms
  - Increased radiolucency (more BLACK on XR)
  - Rapid tapering of hilar vessels
  - Bullae & pneumothorax
  - Widening of the retrosternal airspace
  - Narrow cardiac shadow
- **PULMONARY FUNCTION**
  - **Low FEV1**
  - **High TLC & RV**
- TREATMENT
  - Stop smoking = stop progression
  - Bronchodiators, steroids, bullectomy, transplant

OTHER FORMS OF EMPHYSEMA: ***Compensatory, Obstructive Over-inflation, Bullous, and Interstitial***

BULLOUS EMPHYSEMA with large subpleural bullae, usually located near the **APEX**; may rupture causing **pneumothorax**

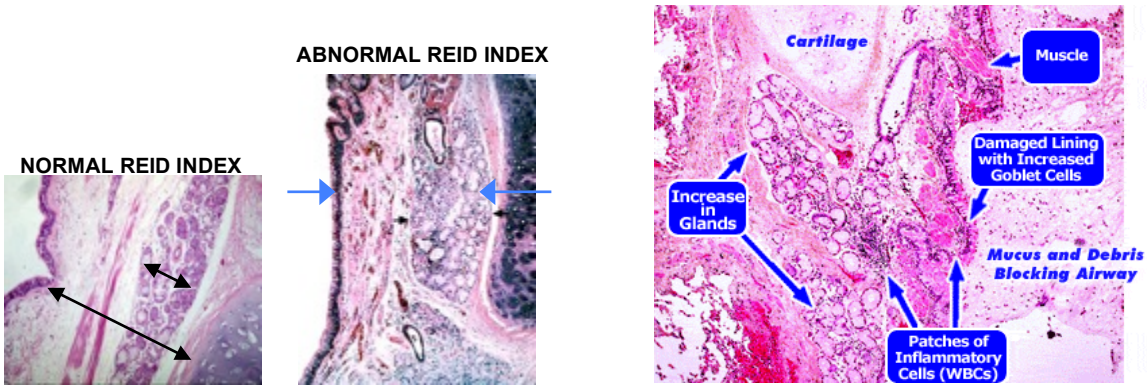


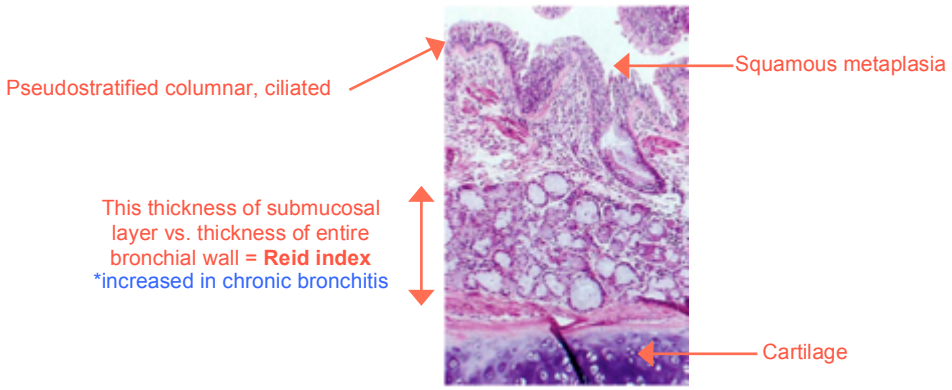
2. CHRONIC BRONCHITIS – "Blue Bloater"

- **Clinical diagnosis** based on productive cough for 3 months in at least 2 consecutive years – *Excessive mucus production leads to mucus plug obstruction*
  - Impaired Gas Exchange + Cyanosis = Blue Bloaters with Hypercapnia + Hypoxemia
- Involves more central/major bronchi
- Primary or initiating factor: chronic irritation by inhaled substances (SMOKING!!), grain, cotton, silica dust
  - **Chronic irritation: squamous metaplasia → dysplasia → squamous cell carcinoma**
- **Common complications**: atelectasis (secondary to bronchiolar mucus plugs), pneumonia

CHRONIC BRONCHITIS: Pathological Findings

- **KEY FINDINGS:**
  - Mucus gland hyperplasia & hypertrophy
  - Excessive mucus production – *obstructs lumen*
  - Goblet cell hyperplasia & metaplasia
- **INCREASED REID INDEX**: ratio of the thickness of the submucosal gland layer to the bronchial wall
  - **> 0.4 in CB**
  - When it is increased → decreases lumen diameter
- **Bronchiolitis obliterans** of small airways – fibrosis & inflammation

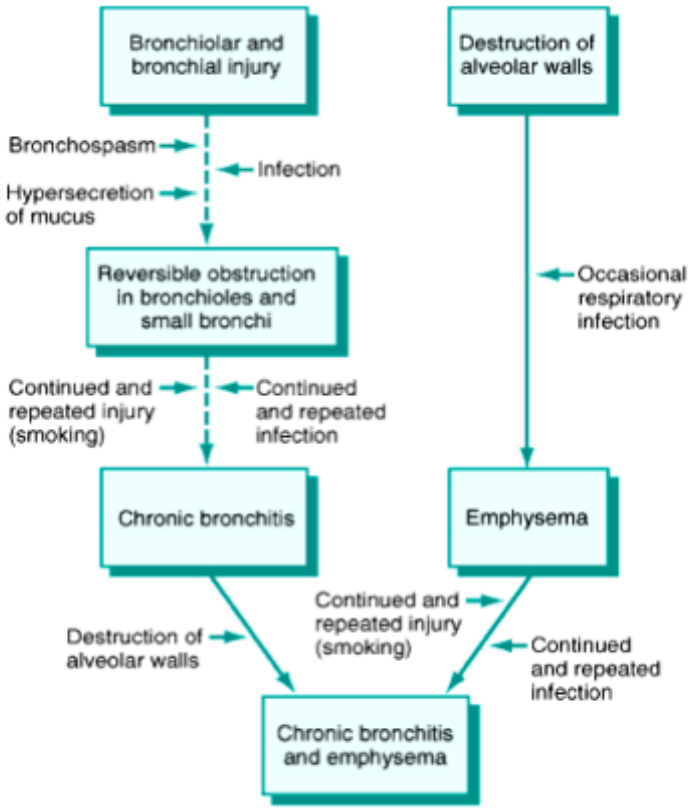




CHRONIC BRONCHITIS: Clinical Manifestations

- Usually in **OLDER, OBESE** patients
- Persistent cough with sputum & superimposed infections
- Mismatching of ventilation & perfusion; increased A-a gradient
- Hypoxemia (cyanosis)
- Respiratory acidosis due to hypercapnia
- Progresses to dyspnea on exertion, COPD, cor pulmonale
- **CHEST X-RAY**
  - Normal
  - Bibasilar increase in bronchovascular markings due to bronchial wall thickening

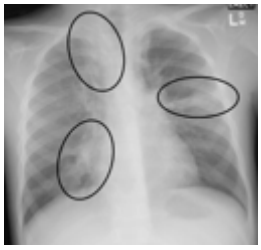
COMPARISON OF EMPHYSEMA & CHRONIC BRONCHITIS



	Pred. Bronchitis	Pred. Emphysema
Age (yr)	40-45	50-75
Dyspnea	Mild; late	Severe; early
Cough	Early; copious sputum	Late; scant sputum
Infections	Common	Occasional
Resp.Insufficiency	Repeated	Terminal
Cor pulmonale	Common	Rare; terminal
Airway resistance	Increased	Normal/sl.increase
Elastic recoil	Normal	Low
Chest radiograph	Prominent vessels, large heart	Hyperinflation, small heart
Appearance	***BLUE BLOATER***	***PINK PUFFER***

3. ASTHMA

- Chronic disease of the conducting airways, usually caused by an immunological reaction & is characterized by episodic bronchoconstriction with inflammation of bronchial walls & excessive mucus secretion
- Recurrent episodes of tachypnea, **wheezing**, breathlessness, chest tightness, & cough



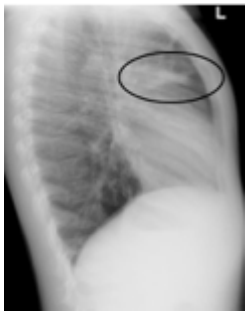
ATOPIC ASTHMA (EXTRINSIC)

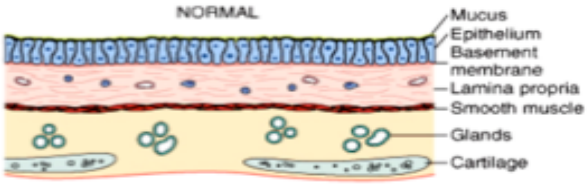
- **MOST COMMON TYPE**
- Begins in childhood
- Environmental agents trigger attacks – *dust, pollen, animal dander, food*
- Type I Hypersensitivity with IgE & mast cell degranulation
- Positive family history of atopy – genetic susceptibility

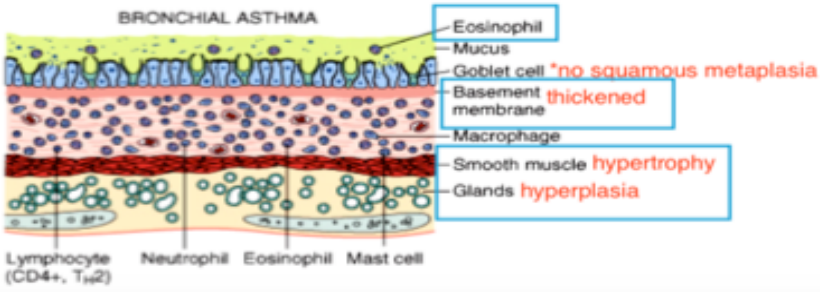
NON-ATOPIC ASTHMA (INTRINSIC)

- Most often induced by viral respiratory tract infections or **ASPIRIN**
  - Aspirin is thought to inhibit COX pathway of arachidonic acid
  - Factors leukotriene production → bronchoconstriction
  - Can also cause Type I allergic type reaction with urticarial
- Also induced by cold, exercise, stress, etc.
- No allergic indicators

LUNG **HYPER-INFLATION**
R UPPER LOBE – PARTIAL COLLAPSE
RLL– SEGMENTAL COLLAPSE
LUL – HORIZONTAL SEGMENTAL COLLAPSE



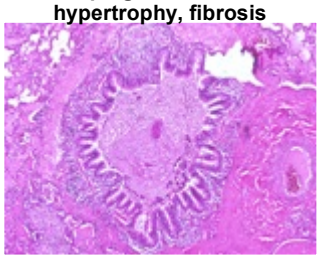




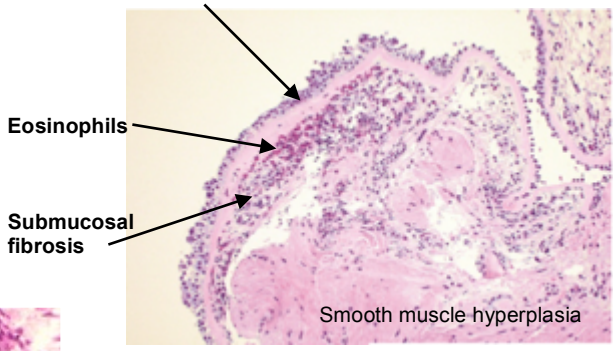
ASTHMA: Pathology

- Epithelial injury
- Occlusion of bronchi & bronchioles by thick tenacious **mucus plugs** – *due to hyperplasia of submucosal glands*
- **CURSCHMANN'S SPIRALS – *sloughed off epithelial cells*
- **CHARCOT-LEYDEN CRYSTALS – *associated with eosinophils/neutrophils*
- Bronchial basement membrane thickening
- Hypertrophy of bronchial wall

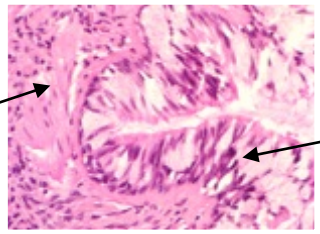
Mucus plug, smooth muscle hypertrophy, fibrosis



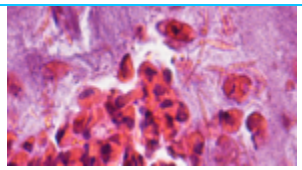
Thickened BM



CURSCHMANN'S SPIRALS



CHARCOT-LEYDEN CRYSTALS

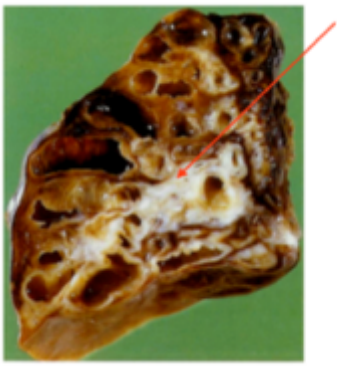


4. BRONCHIECTASIS

- *A disorder in which smooth muscle cells & elastic tissue are destroyed by chronic **necrotizing infections** & lead to **permanent (irreversible) dilation of the bronchi** & bronchioles*
- Obstruction & infection are major influences on bronchiectasis
  - **ANAEROBIC** bacterial growth in areas blocked by obstruction – *When you release the plug, **foul-smelling sputum***
- **COMPLICATIONS**: atelectasis, pneumonia (lung abscesses), cor pulmonale, secondary amyloidosis
- **PRE-DISPOSING FACTORS**
  - Bronchial obstruction – *tumor, FB, chronic bronchitis, cystic fibrosis, pneumonia due to aspergillus or pseudomonas*
  - Immunodeficiency states
  - Primary ciliary dyskinesia
    - **KARTAGENER SYNDROME**: immobile cilia; bronchiectasis, sinusitis, sinus inversus
  - Post-infectious states
  - ***ALCOHOLISM** – more prone to aspiration → abscess formation, aspiration pneumonia*

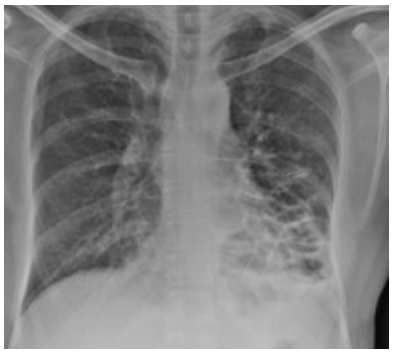
BRONCHIECTASIS: Morphology

- Cystically dilated bronchi filled with pus (mucopurulent secretions)
- Dilation extending to the periphery of the lung – *pleural spaces*
- **PROXIMAL RESPIRATORY TRACT DILATION**

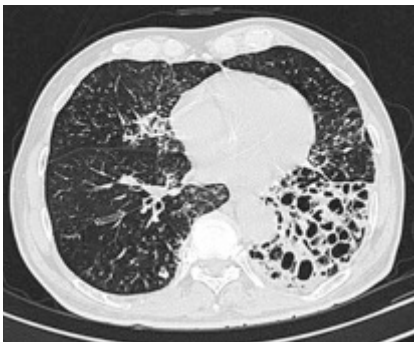


Cartilage around the dilated structures tells us it's not emphysema!

AP CXR

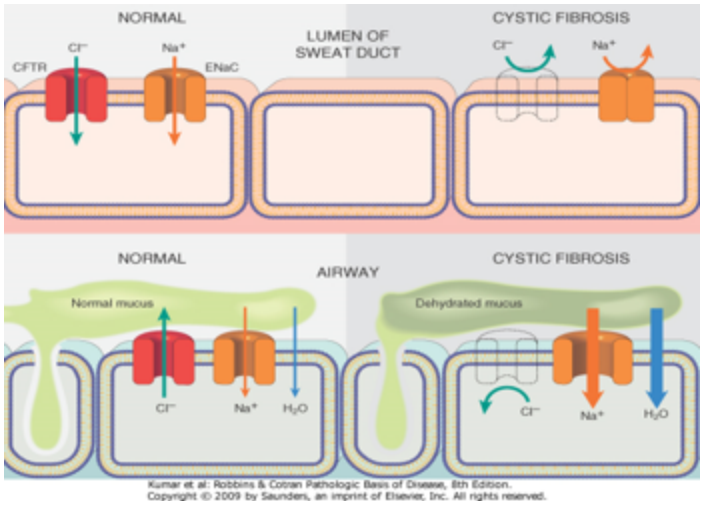


AXIAL CT



CYSTIC FIBROSIS (MUCOVISCIDOSIS)

- AR inherited disorder of ion transport that affects fluid secretion in exocrine glands & the epithelium of the respiratory (tracheobronchial tree + sinuses), GI (gut+liver), & reproductive tracts with phenotypic variation
- **Causes**: Abnormal function of an epithelial Cl^- channel coded by the **CFTR** gene on Chromosome 7q31.2
  - In conjunction with ENaC (epithelial sodium channel)



CYSTIC FIBROSIS
1. Increased sodium & water reabsorption
2. Dehydration of the mucus layer with defective mucociliary action & mucus plugging of airways.

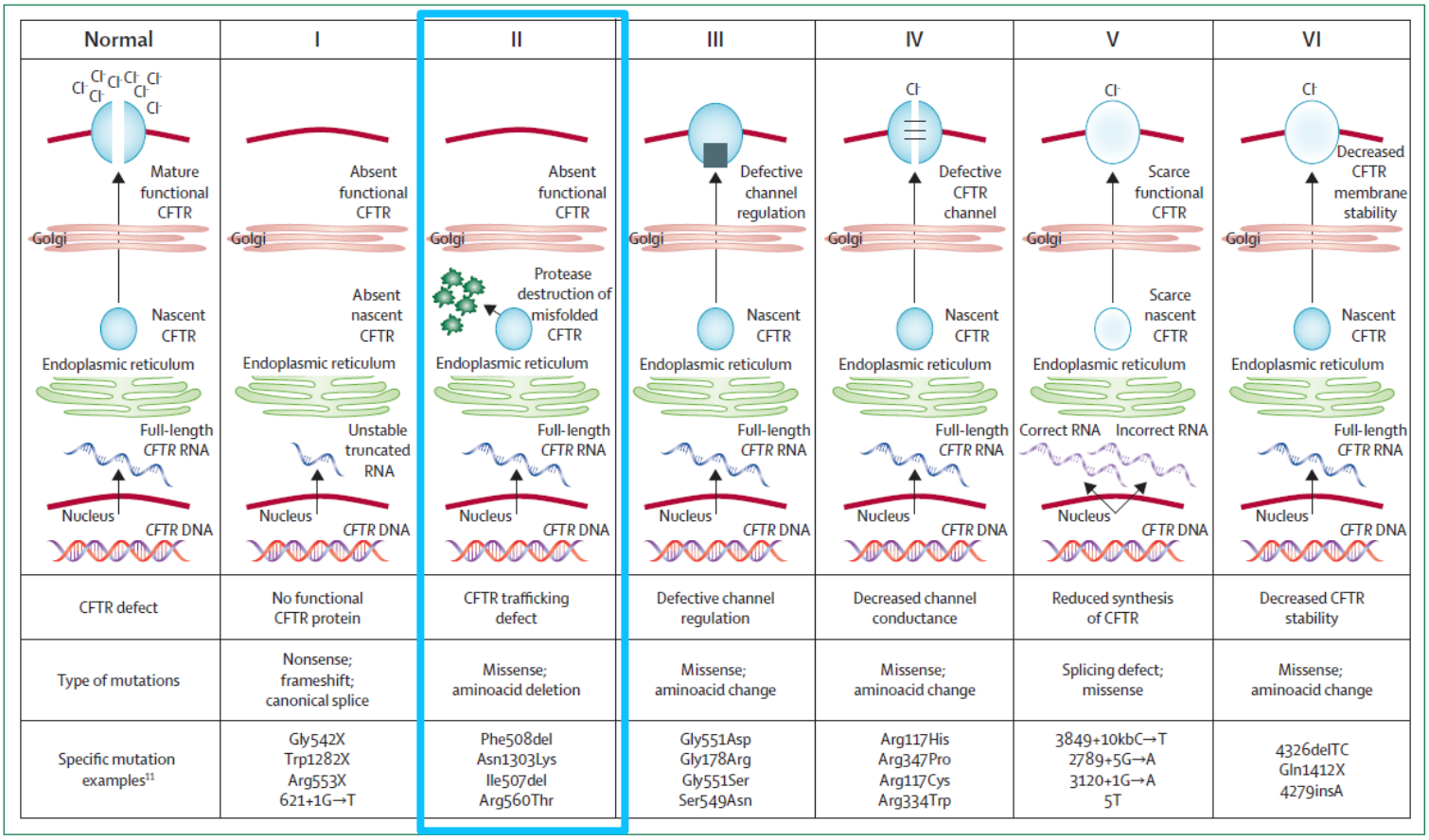


Figure 1: Classes of *CFTR* mutations

CLASSES OF CYSTIC FIBROSIS

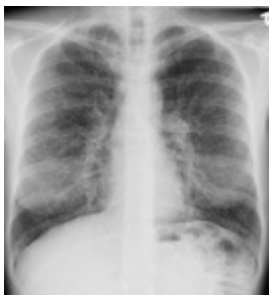
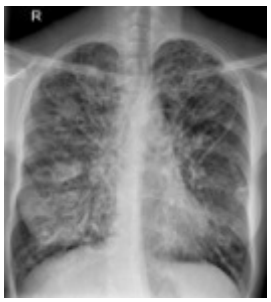
- **Class I**: *Defective protein synthesis.* **Complete lack** CFTR.
- **Class II** *most common: *Abnormal protein folding, processing, and trafficking.* **Most common (ΔF508) gene mutation in 70% of patients**. **Complete lack** CFTR.
- **Class III**: *Defective regulation.* CFTR **nonfunctional**.
- **Class IV**: *Decreased conductance.* CFTR **reduced** function.
- **Class V**: *Reduced abundance.* **Reduced** normal protein.
- **Class VI**: *Altered regulation of separate ion channels.* Affect the regulatory role of CFTR.

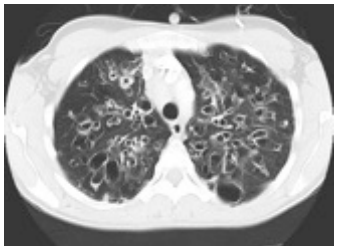
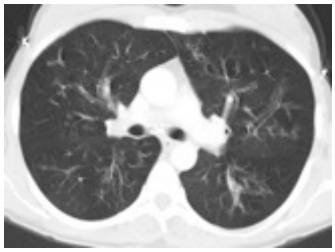
CYSTIC FIBROSIS: CHEST X-RAY

- Course interstitial markings
- Nodularities

CYSTIC FIBROSIS: HRCT

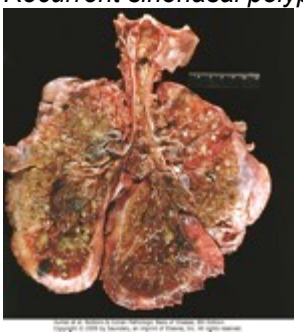
- Nodular densities in periphery
- Tree-in-bed pattern
- Bronchial wall thickening
- Bronchiectasis

CYSTIC FIBROSIS: Clinical

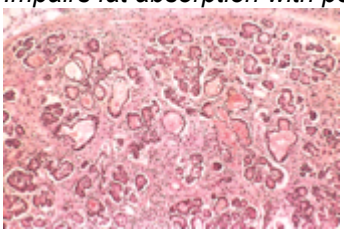
- **LUNGS & HEART**
  - Most common cause of death in CF
  - Hyperplasia & hypertrophy of the mucus cells producing viscous mucus with secondary obstruction
  - *Infections give rise to severe chronic bronchitis, bronchiectasis, lung abscesses*
  - *Usually **Staph. aureus**, H. influenza, & **Pseudomonas aeruginoas** (including a mucoid form – alginate producing)*
  - *May lead to cor pulmonale*
  - *Recurrent sinonasal polyps*



LUNGS OF A PATIENT WITH CYSTIC FIBROSIS
There is extensive mucus plugging & dilation of the tracheobronchial tree. The pulmonary parenchyma is consolidated by a combination of both secretion & pneumonia – *the green color is associated with Pseudomonas*

***80% of patients with CF die of cardiorespiratory disease**
OBSTRUCTIVE LUNG DISEASE +/- COR PULMONALE

- **PANCREAS**
  - 85-90% of patients with severe CF lose exocrine function
  - *Ducts are plugged with inspissated mucus; the glands become dilated & atrophic; the parenchyma becomes fibrotic; Islets are spared → LOSS OF FAT ABSORPTION*
    - *Pancreatic achylia with malabsorption, inanition, & stunted development*
    - *Impairs fat absorption with possible avitaminosis A, D, or K & squamous metaplasia of the ducts*



PANCREAS OF A PATIENT WITH CYSTIC FIBROSIS
Mild to moderate changes – The ducts are dilated & plugged with eosinophilic mucin, & the parenchymal glands are atrophic & replaced by fibrous tissue.

- INTESTINES: meconium ileus of infants, rectal prolapse
- LIVER: bile canaliculi plugged, ductular proliferation, portal inflammation, steatosis, focal biliary cirrhosis
- SALIVARY GLANDS: dilation of ducts, squamous metaplasia & glandular atrophy
- AZOOSPERMIA & INFERTILITY: 95% of males usually have **congenital bilateral absence of vas deferens**

CYSTIC FIBROSIS: Diagnosis

- One or more characteristic phenotypic features OR a history of CF in a sibling, OR + newborn screen test
- **PLUS** increased sweat chloride concentration on 2 or more occasions OR identification of 2 CFTR mutations OR demonstration of abnormal epithelial nasal ion transport

CYSTIC FIBROSIS: Treatment

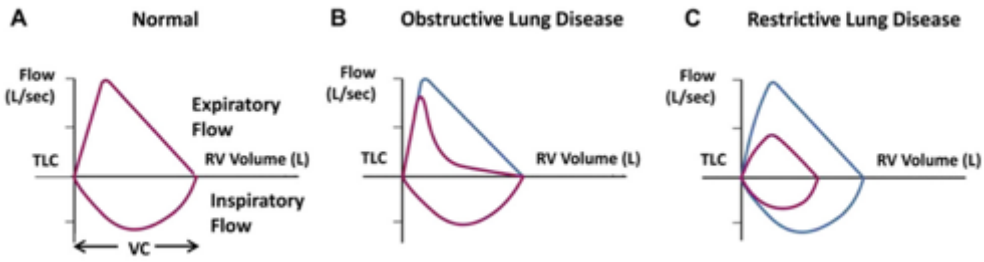
- PANCREATIC INSUFFICIENCY
  - Oral pancrelipase (lipase, protease, amylase)
  - Treat DM if islets destroyed (uncommon)
- VITAMIN DEFICIENCY
  - Oral fat soluble vitamins (A, D, E, K)
    Parenteral nutrition
- PULMONARY DISEASE
  - Postural drainage & chest percussion
  - Bronchodilators (Albuterol)
  - Mucocytic agents – inhaled acetylcysteine breaks down mucoproteins, inhaled dornase alfa breaks down DNA
  - Antibiotics
  - Hypertonic saline (inhaled)
  - High dose ibuprofen – slows lung disease progression
  - LUNG TRANSPLANTS

RESTRICTIVE LUNG DISORDERS

- Restrictive lung disorders occur in 2 general conditions:
  - **Chronic interstitial & infiltrative diseases** – pneumoconiosis & interstitial fibrosis of unknown etiology
  - **Chest wall disorders** – neuromuscular disorders such as poliomyelitis, severe obesity, pleural diseases, & kyphoscoliosis

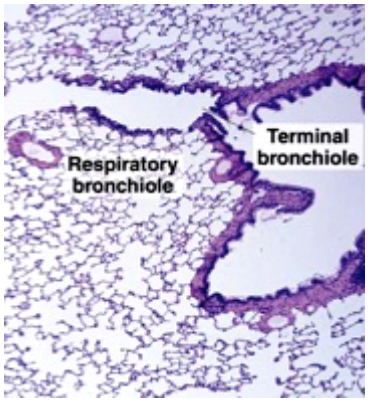
CHRONIC INTERSTITIAL LUNG DISEASE

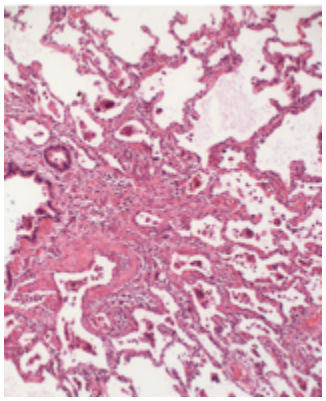
- Heterogeneous group of disorders characterized predominantly by inflammation & fibrosis of pulmonary interstitium leading to reduce lung compliant & diffusion defect
- **CLINICAL FEATURES** – *dyspnea, tachypnea, & cyanosis*
- PULMONARY FUNCTION - ↓FVC, normal FEV1/FVC ratio



INTERSTITIAL LUNG DISEASE – Chest X-Ray

- BILATERAL LESIONS (EARLY)
  - Small nodules, irregular lines, ground glass shadows
- BILATERAL LESIONS (LATE)
  - **HONEYCOMB LUNGS**

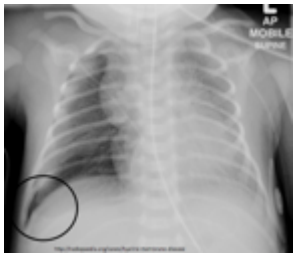




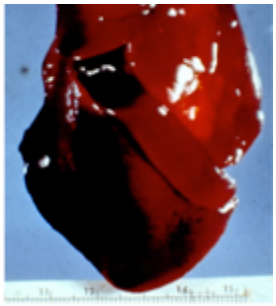
ACUTE ILD – ARDS	CHRONIC ILD
Newborn Acute Respiratory Distress Syndrome **Adult Acute Respiratory Distress Syndrome**	**KNOWN CAUSE – *occupational, infections, allergens*** **Pneumoconioses (Antracosis, Asbestosis, Silicosis)** Extensive allergic alveolitis **(Hypersensitivity Pneumonia)** Iatrogenic ILD caused by drugs or radiation **IDIOPATHIC (65%)** **Usual Interstitial Pneumonia (UIP), Non-specific Interstitial Pneumonia (NIP),** Respiratory Bronchiolities ILD in **smokers**, Desquamative Interstitial Pneumonia (DIP) Cryptogenic Organizing Pneumonia (COP)/Bronchiolitis Obliterans(BOOP), Lymphoid Interstitial Pneumonia (LIP), **Acute Interstitial Pneumonia (AIP)** **Sarcoidosis** **SYSTEMIC AUTOIMMUNE DISEASES** ILD in Rheumatic Arthritis ILD in Progressive Systemic Sclerosis

NEONATAL ACUTE RESPIRATORY DISTRESS SYNDROME (ARDS)

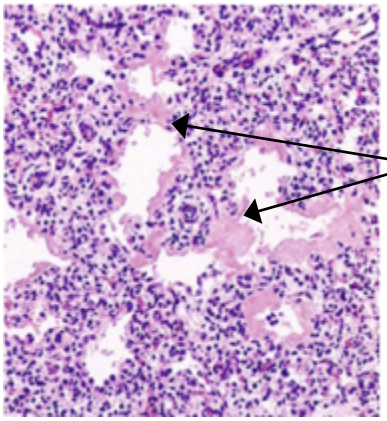
- *Hyaline membrane disease because of the deposition of a layer of hyaline proteinaceous material in the peripheral airspaces of newborns*
- Damage to endothelial & alveolar epithelial cells with inflammation are the **key initiating events** & basis of lung damage
- The characteristic **HISTOLOGY** is that of **hyaline membranes** lining alveolar walls
  - Edema, scattered neutrophils & macrophages, & epithelial necrosis are also present
- **RISK FACTORS:** *preterm newborn, male gender, maternal diabetes, & cesarean section*
- **ETIOLOGY:** immature lungs with insufficient surfactant
- **TREATMENT:** prevent delivery until the lung is mature (amniocentesis), exogenous surfactants, manage ventilation & blood gases
- **COMPLICATIONS:** retinopathy (retolental fibroplasia), bronchopulmonary dysplasia
- **Pre-term complication:** patent ductus arteriosus, cerebral intraventricular hemorrhage, & necrotizing entercolitis



NEONATAL RESPIRATORY DISTRESS SYNDROME
Lung fields show diffuse ground glass densities.
Small pneumothorax – no markings.



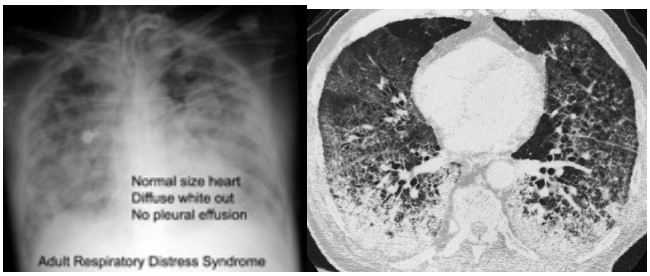
NEONATAL ARDS
Lungs – heavy & dark red



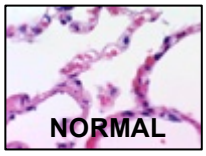
NEONATAL ARDS
Immature lung tissue with hyaline membranes

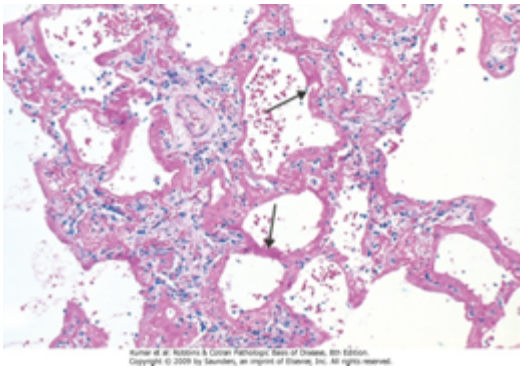
ADULT ACUTE RESPIRATORY DISTRESS SYNDROME

- ARDS is a clinical syndrome of progressive respiratory insufficiency caused by **diffuse damage to alveolar capillaries** in the setting of **severe disease**, including sepsis, severe traumatic injury, multiple transfusions, diffuse pulmonary infection, near drowning, or drug overdose; *or it could be Idiopathic due to AIP*
- ARDS is severe Acute Lung Injury (ALI)
  - *Lung injury of acute onset, within one week of an apparent clinical insult & with progression of respiratory symptoms*
- **CLINICAL**: dyspnea & tachypnea with a rapid onset; decreased arterial P_aO_2/F_iO_2 ratio; bilateral opacities on chest imagining not explained by any other pulmonary pathologies
- Many factors, including NKFβ, IL-8, IL-8, TNF, & **neutrophilic migration**
- *The alveolar capillary membrane is formed by 2 separate barriers: the microvascular endothelium & the alveolar epithelium. In ARDS, the integrity of this barrier is compromised by either endothelial or epithelial injury, or both.*
- **Secondary loss of surfactant**



ACUTE RESPIRATORY DISTRESS SYNDROME – multifocal bilateral air-space opacities predominantly **PERI-HILAR & LOWER ZONE** distribution

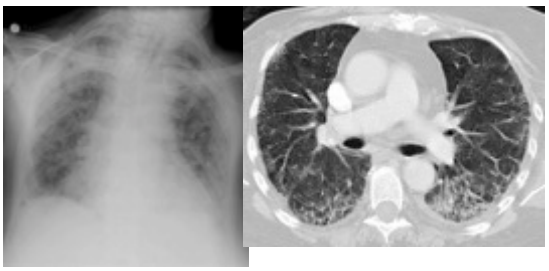




ACUTE RESPIRATORY DISTRESS SYNDROME – some of the alveoli are collapsed; others are distended, & many are lined by hyaline membranes (arrows)
Hyaline comes from inspissation of protein rich edema – surrounds debris of dead alveolar epithelial cells

ACUTE INTERSTITIAL PNEUMONIA (AIP) – ILD

- *AIP is a term used to describe widespread Acute Lung Injury of unknown etiology associated with a rapidly progressive clinical course. It is an uncommon disorder that occurs at the mean age of 59 & has no sex predilection. Patients present with acute respiratory failure often following an illness of less than 3 weeks duration that resembles an upper respiratory tract infection. (Robbins)*
- A **rapidly progressive** interstitial pneumonia of unknown etiology that occurs in **HEALTHY INDIVIDUALS** without a history of lung disease, who present *within days to weeks* following the onset of symptoms
- AKA **Hamman-Rich Syndrome**, Accelerated Interstitial Pneumonitis, Idiopathic Respiratory Distress Syndrome
- **PATHOLOGY**
  - Hyaline membranes with interstitial fibrosis & organizing pneumonia – *This is the pattern of **Diffuse Alveolar Damage (DAD)***
  - Exudative phase – alveolar septal edema & hyaline membranes along alveolar walls
  - Proliferative phase – intraalveolar & interstitial organization
  - Fibrotic phase – alveolar septal fibrosis
- **CHEST X-RAY: bilateral patchy airspace opacitie**
- **HRCT:**
  - GROUND GLASS ATTENUATION
    - Bilateral, patchy, & diffuse
    - With or without airspace consolidation
    - Geographic distribution with spared areas



INTERSTITIAL LUNG DISEASE OF KNOWN ETIOLOGY

Coal Worker's Pneumoconiosis, Silicosis, Asbestosis, Hypersensitivity Pneumonitis, Drugs/Radiation, Fumes/Vapors

CLEARANCE OF DEPOSITED PARTICLES

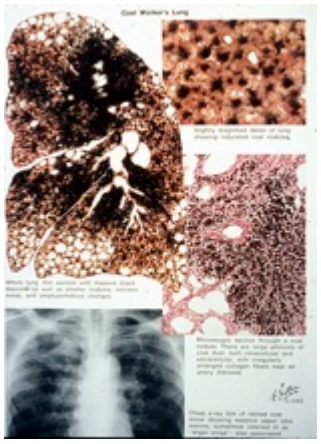
- Mucociliary system transports particles
- Alveolar macrophages engulfs particles
- Mucociliary escalator

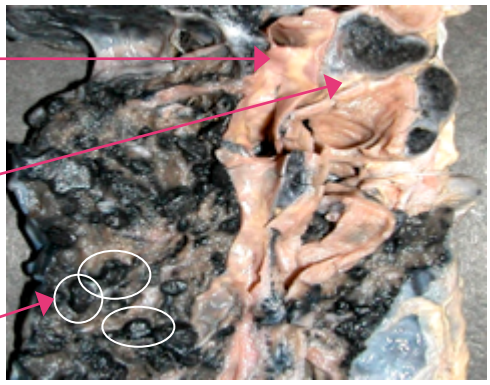
PNEUMOCONIOSIS – Fibrosing ILD

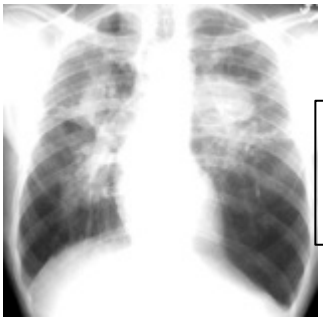
- *'Pneumoconiosis' originally described the non-neoplastic lung reaction to inhalation of mineral dusts encountered in the work place; now it also includes diseases induced by organic, as well as inorganic, particulates & chemical fumes & vapors*
- **KEY PATHOGENETIC FACTORS RELATING TO INHALED PARTICLES:**
  - **Size (1-5 µm), Solubility, Concentration**

1. COAL WORKER'S PNEUMOCONIOSIS – Fibrosing ILD

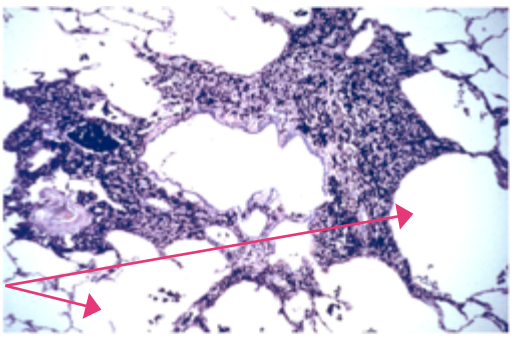
- **"BLACK LUNG" DISEASE** – From inhalation of coal dust in large amounts to produce "coal macules"
- Disease ranges from:
  - **ASYMPTOMATIC ANTHRACOSIS** – *Not fibrogenic; anthracotic pigmentation*
    - Most innocuous coal-induced pulmonary lesion in **COAL MINERS** & to some degree in urban dwellers & tobacco smokers
    - Inhaled carbon pigment is engulfed by alveolar or interstitial macrophages, which then accumulate in the CT along the lymphatics or in organized lymphoid tissue along the bronchi or in the lung hilus
  - **Simple coal worker's pneumoconiosis** – *macules and nodules +/- centrilobular emphysema & disease from smoking*
  - Complicated coal worker's pneumoconiosis (**Progressive Massive Fibrosis**-PMF) – *pulmonary dysfunction w/ pulmonary HTN & cor pulmonale*
  - **Caplan Syndrome** = Black lung + RA
- In most cases, **CARBON DUST** itself is the major culprit, but contaminating silica in the coal dust can favor progressive disease





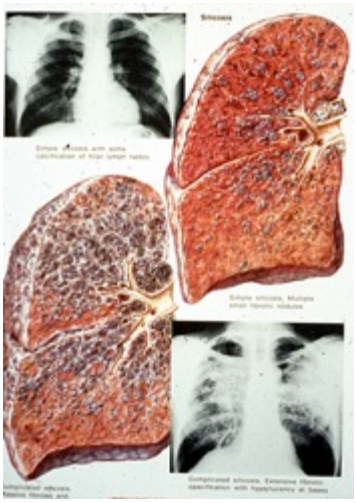


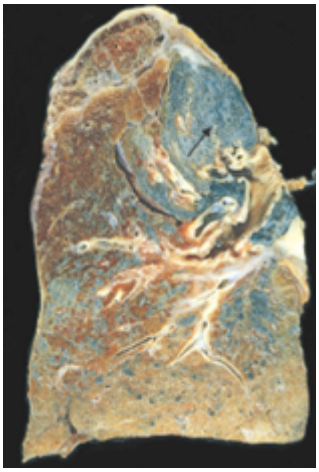
PROGRESSIVE MASSIVE FIBROSIS
*A form of **silicosis** characterized by **dense agglomeration of nodules** causing massive **scarring** usually in the UPPER LOBES*



2. SILICOSIS – Pneumonoultramicroscropicsilicovolcanoconiosis – Fibrosing ILD

- **Most prevalent occupational disease**; caused by inhalation of minerals with silicates, such as quartz or talc
- Produces silicotic nodules throughout the lung
- Usually presents **after DECADES** of exposure as a ***slowly progressing, nodular, fibrosing pneumoconiosis***
  - *Cases: Older woman who worked in the sand industry for 10 years & c/o SOB for 3 years*
- **SANDBLASTERS** (to clean steel) & miners
- **Patients have increased risk for lung cancer (1**.5-2x average) & for **Tuberculosis**
- **PATHOGENESIS**: particles are phagocytized & within the macrophages, silica causes activation & release of inflammatory mediators (IL-1, TNF, fibronectin, etc.)
- Silicosis is characterized grossly in its early stages as **tiny, discrete, pale nodules → blackened, hard, collagenous scars** in the **UPPER LOBES** of the lungs.
- **Fibrotic lesions** may also occur in the lymph nodes & are seen radiographically as **EGGSHELL CALCIFICATIONS –** *Fine calcifications seen at the periphery of a mass & usually relating to lymph node calcification* **(in HILAR LYMPH NODES)**

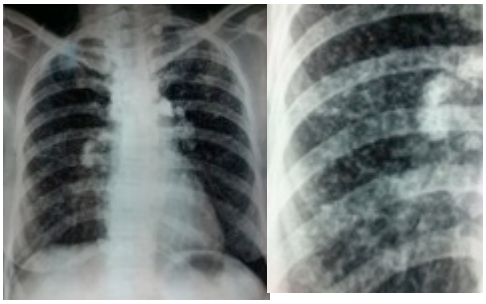


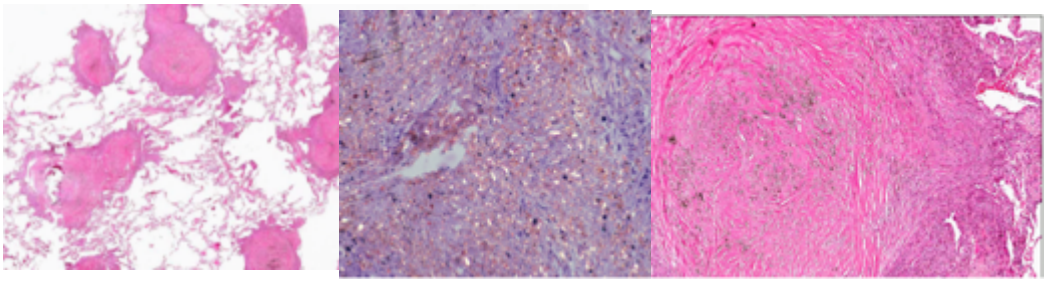


SILICOSIS
Scarring has contracted the **UPPER lobe** into a small dark nodules (*arrow*). Note the **dense pleural thickening**.

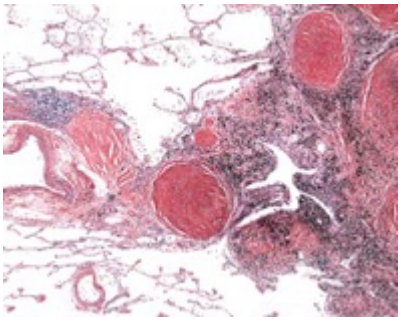
SILICOTIC NODULES

EGGSHELL CALCIFICATIONS IN HILAR LYMPH NODES





SILICOTIC NODULES
Polarizing light – birefringent silica

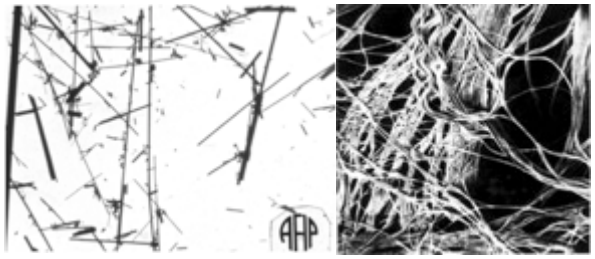


SILICOSIS
MILIARY mottling – *"seed-like"*
PERI-HILAR & MEDIASTINAL lymphadenopathy showing **"EGG SHELL CALCIFICATION"**

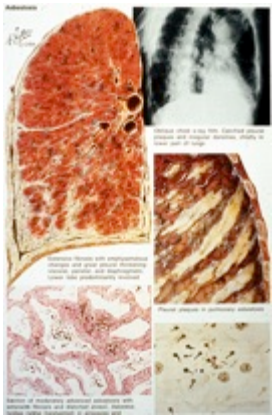
3. ASBESTOSIS – Fibrosing ILD

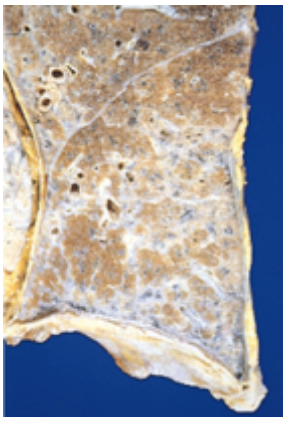
- Asbestosis produces diffuse interstitial fibrosis **over a period of DECADES**
- Seen in **SHIPYARD WORKERS, ROOFERS**
- **PATHOGENESIS**: particles are phagocytized & there is a release of inflammatory mediators, which eventually produce fibrosis
  - **AMPHIBOLE-TYPE** is the most pathogenic – ***STRAIGHT, NEEDLE-LIKE CRYSTALS***
  - ***Serpentine crystals*** *account for most of the asbestos used in industry*
- Involves the **LOWER LOBES** greater than the upper lobes
- NO LYMPH NODES as seen in silicosis
- Causes **diaphragmatic pleural plaques**
- **MORPHOLOGY:** Asbestosis is marked by **diffuse pulmonary interstitial fibrosis**, which is indistinguishable from diffuse interstitial fibrosis from other causes, except for the presence of multiple **asbestos bodies**
  - **ASBESTOS BODIES** appear as golden brown, fusiform or beaded rods with a translucent center & consists of asbestos fibers coated with iron-containing proteinaceous material – **"DUMBELL SHAPED"**
  - Associated with **FERRUGINOUS BODIES**
    - Fibers of asbestos coated in iron-rich material from proteins like ferritin & hemosiderin
    - Formed by macrophages who have phagocytized the fibers trying to digest them
- Increased risk for **MESOTHELIOMA** (associated only with amphibole asbestos fibers) & **BRONCHOGENIC CARCINOMA**, *especially in SMOKERS*

Amphibole Asbestos Fibers (straight)
→ MESOTHELIOMA

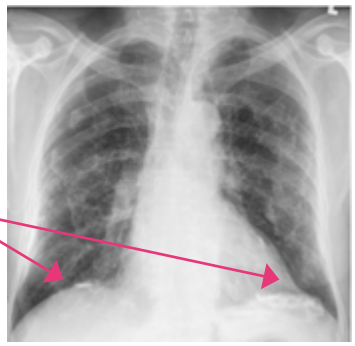


Sepentine Thrysotile Fibers



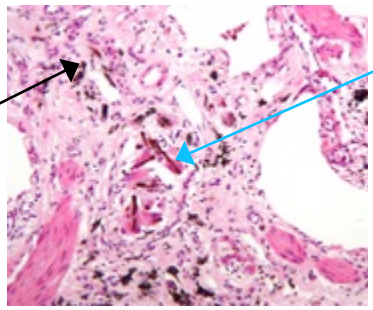


CALCIFIED PLAQUES

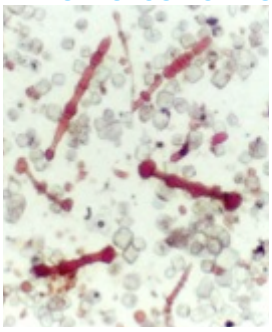


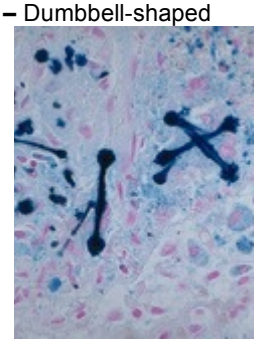
Fibrosis

Asbestos Bodies

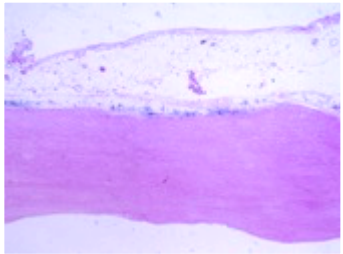


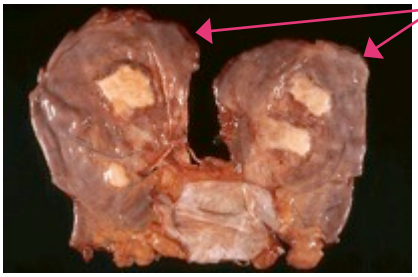
ASBESTOS BODIES – Dumbbell-shaped





PLEURAL PLAQUES
No asbestos bodies!



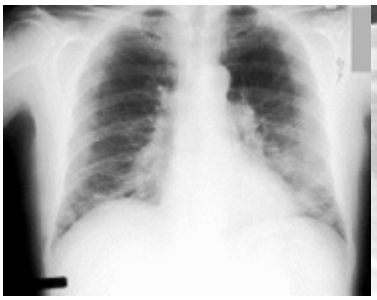


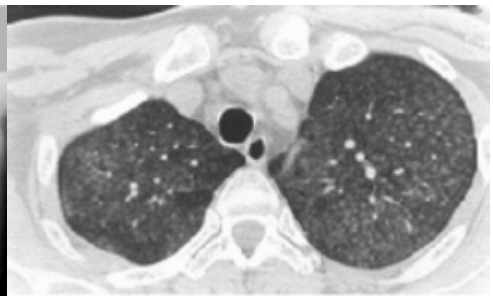
DIAPHRAGMATIC PLEURAL PLAQUES

4. HYPERSENSITIVITY PNEUMONITIS (Extrinsic Allergic Alveolitis) – Granulomatous ILD

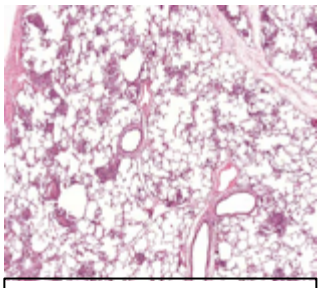
- Immunologically mediated response to an extrinsic antigen that involves both immune complex & delayed-type hypersensitivity (HSR 3 & 4)
- Results from the inhalation of organic dust containing antigens made up of **spores of thermophilic bacteria, true fungi, animal proteins, or bacterial products**
- **FARMER'S LUNG**
  - **MOLDY HAY** with spores is inhaled – organism is **ACTINOMYCES** (or fungal Ag, like *Aspergillus*)
- **"PIGEON BREEDER'S LUNG**
  - **Pigeon** serum proteins in droppings
- **CLINICAL:** acute onset with fever/chills within **HOURS** after exposure; or chronic w/ cough & dyspnea
- **LAB**: serum precipitins (antibodies) to a suspected antigen
- **PATHOLOGY: VASCULITIS/FIBRINOID NECROSIS** (HSR 3) and/or **GRANULOMAS** (HSR 4) on biopsy
- **TREATMENT:** removal of environmental agent
  - *It is important to recognize these diseases early in the course because progression to serious chronic fibrotic lung disease can be prevented by removal of the environmental agent*
- **COMPLICATION:** Interstitial pneumonitis & fibrosis, if chronic

Interstitial markings in the BASES

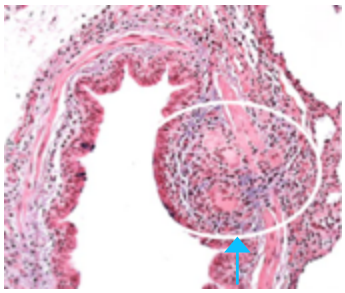




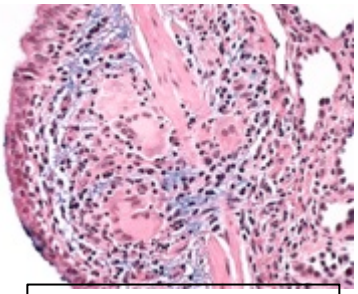
UPPER LOBE NODULAR PATTERN in chronic disease



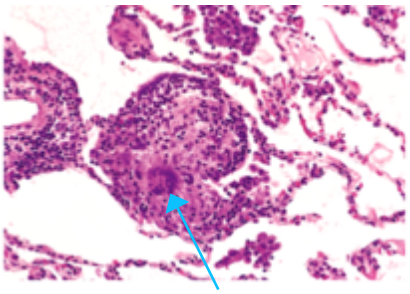
PATCHY INFILTRATE



MICROGRANULOMA



MICROGRANULOMA



GIANT CELL

5. DRUG/RADIATION ILD – Fibrosing ILD

- Cytotoxic drugs: bleomycin (pneumonitis & fibrosis), methotrexate (hypersensitivity pneumonitis)
- Amidarone (pneumonitis & fibrosis), Nitrofurantoin (hypersensitivity pneumonitis), Aspirin & β-antagonists (bronchospasms)
- **RADIATION PNEUMONITIS**
  - ACUTE: in 10-20%, with lymphocyte alveolitis or hypersensitivity pneumonia, pleural effusions & infiltrates on XR within 6 months of radiation
  - CHRONIC: pulmonary fibrosis (looks like diffuse alveolar damage)

6. AIR POLLUTION – INHALED TOXINS

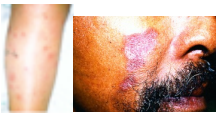
- Toxic fumes or vapors: NO_2, ozone, SO_2, chlorine, hydrocarbons (toluene), cyanates, ammonia, cadmium, mercury → acute pneumonitis (mild to severe), contribute to obstructive pulmonary diseases (bronchitis, asthma, emphysema)
- Persons at greatest risk: underlying lung disease, poor health
- **RADON GAS: second most common cause of lung cancer;** seeps from soil in many areas of US

INTERSTITIAL LUNG DISEASE OF UNKNOWN ETIOLOGY/IDIOPATHIC

Sarcoidosis, Usual Interstitial Pneumonitis (UIP/IFP) Non-specific Interstitial Pneumonitis (NSIP)

1. SARCOIDOSIS – Granulomatous ILD

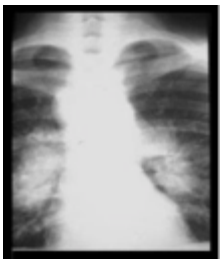
- Typically seen in **YOUNG (20-40 y/o) AFRICAN AMERICAN FEMALES**
- Most commonly affects **LUNGS*, SKIN, LYMPH NODES, liver, bone marrow, spleen**
  - Can involve the heart → **Restrictive Cardiomyopathy**
  - **DERMATOLOGIC MANIFESTATIONS**
    - Non-specific – **ERYTHEMA NODOSUM**
      - Hypersensitivity reaction to many stimuli
      - Tender, subcutaneous nodules, often on the **anterior tibia**
    - Specific – **nodules & papules with granulomas**



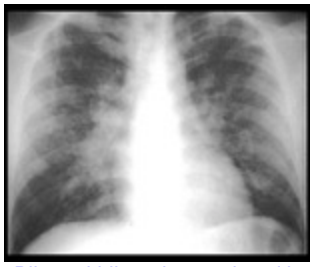
- **CHEST X-RAY: Bilateral HILAR LYMPHADENOPATHY – "ANGEL WING APPEARANCE"**
- **PATHOLOGY:**
  - **SCHAUMANN BODIES –** *small, round calcifications within the granuloma*
  - **ASTEROID BODIES** – *stellate ("star") lesions, engulfed by the giant cells within the granuloma*
  - **NON-CASEATING GRANULOMAS**
    - Aggregations of tightly clustered epithelioid cells (activated macrophage) with **giant cells**
    - *NO eosinophilic caseating necrosis in center!!*
- **DIAGNOSIS**: requires demonstration of non-caseating granulomas ***(diagnosis of exclusion)***
- **SEROLOGIC TESTS: hypercalcemia & elevated ACE**
  - Hypercalcemia → calcium deposits in granulomas (METASTATIC CALCIFICATION)

ANGIOTENSIS CONVERTING ENZYME (ACE)

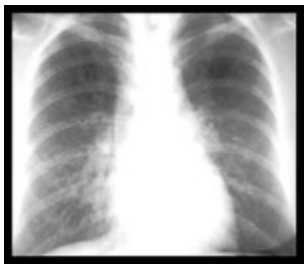
- Elevated in **sarcoidosis & leprosy** (& Gaucher's, primary biliary cirrhosis, amyloidosis, hyperthyroidism, diabetes, acute hepatitis)
  - Levels usually not elevated in other forms of granulomatous lung disease!
- Produced by lung endothelial cells
- Levels higher with **ACTIVE SARCOIDOSIS** (*verses inactive*) – used in diagnosis & monitoring of disease



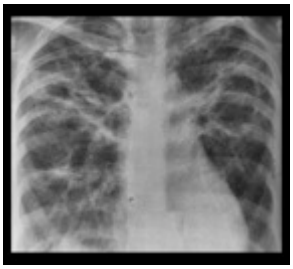
Bilat. hilar adenopathy w/ no parenchymal abnormalities



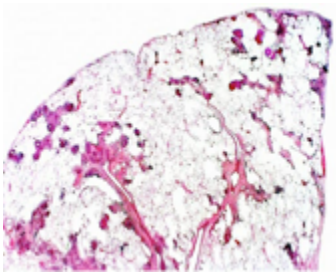
Bilateral hilar adenopathy with diffuse parenchymal changes

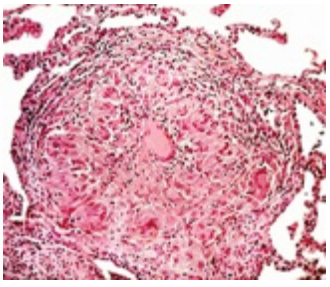


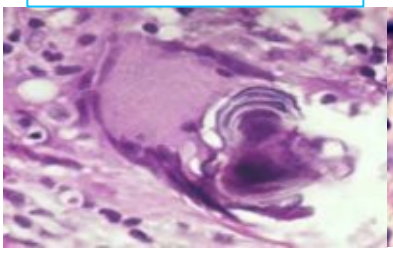
Diffuse parenchymal changes, but no hilar adenopathy

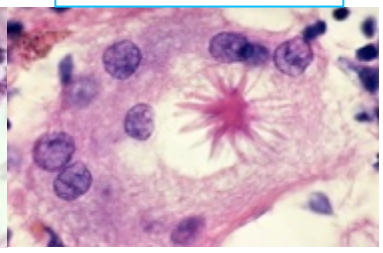


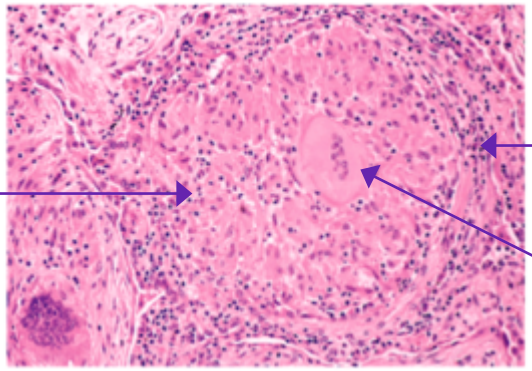
Permanent lung fibrosis



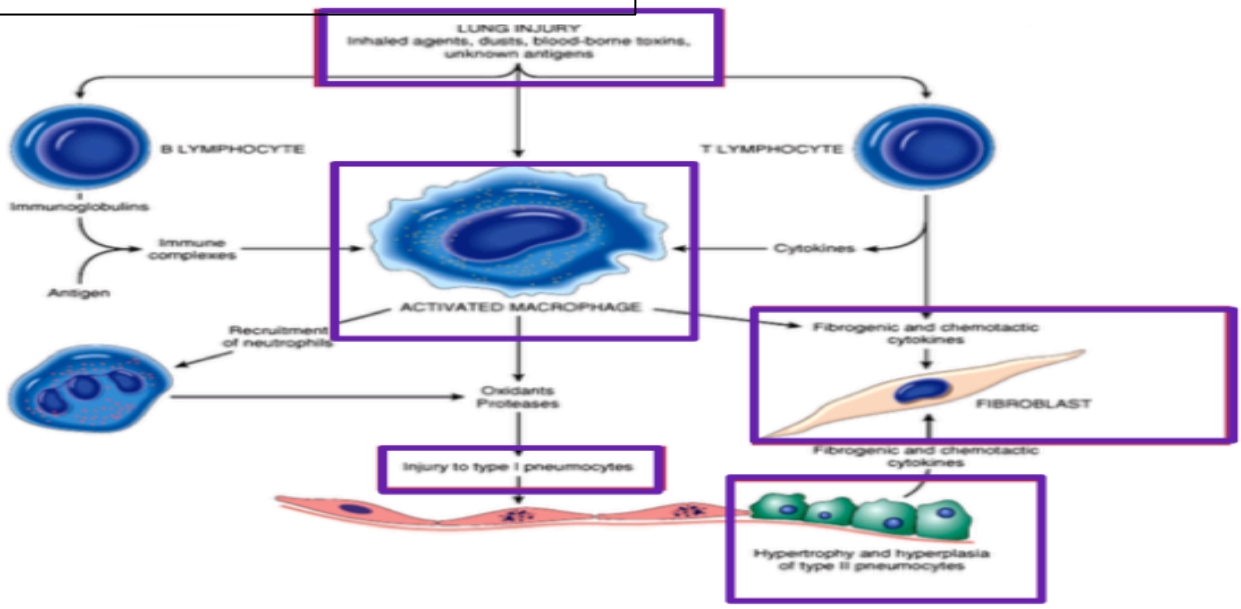






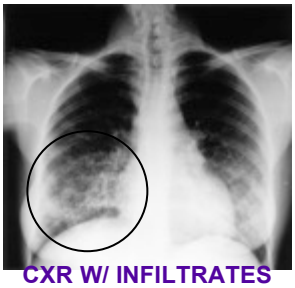


PATHOGENESIS OF CHRONIC RESTRICTIVE LUNG DISEASE

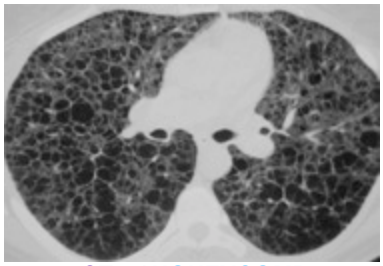


2. USUAL INTERSTITIAL PNEUMONITIS (UIP) – Fibrosing ILD

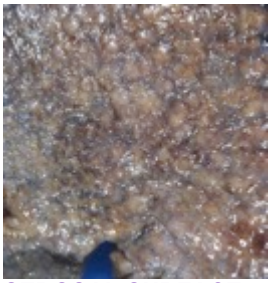
- AKA **Idiopathic Pulmonary Fibrosis (IPF)**
- 55% of Idiopathic ILDs
- Seen in patients **OVER 50 YEARS OLD** & often **MALE**
- Suspected causes: inorganic/organic dusts; autoimmune; drug & radiation therapy
- **CLINICAL: GRADUAL** onset of dyspnea with a cough; increasing fatigue + SOB; eventual **pulmonary HTN**
- **CHEST X-RAY: interstitial infiltrate & later honeycomb lung**
- **PATHOGENESIS**: repeated injury with **scarring**
- **PATHOGENESIS**
  - GROSS – scarring w/ thickened alveolar wall
  - MICROSCOPY – **Temporal Heterogeneity** *(identification of fibrotic lesions at different stages within the same biopsy specimen)*: **patchy interstitial fibrosis**, focal chronic inflammation, focal normal alveoli, & **HONEYCOMB FIBROSIS;** Cobblestoned pleural surfaces
- **TREATMENT: LUNG TRANSPLANT**



CXR W/ INFILTRATES

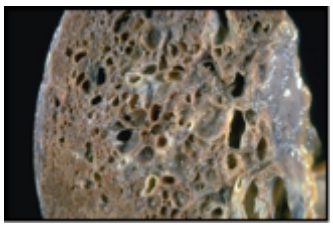


CT w/ HONEYCOMB

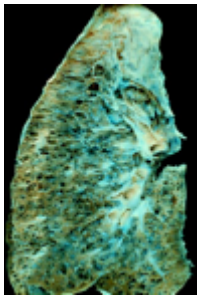


SEROSAL SURFACE

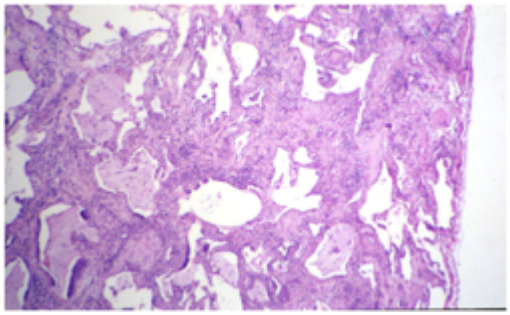
Cut surface w/ SCARRING



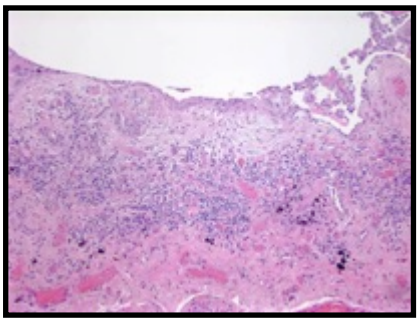
HONEYCOMB LUNG
End stage fibrosis



HONEYCOMB LUNG
End stage fibrosis

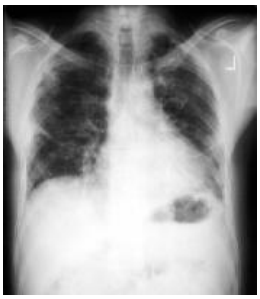
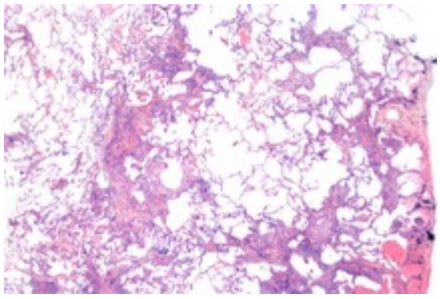


TEMPORAL HETEROGENEITY



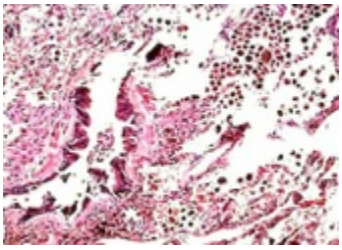
3. NON-SPECIFIC INTERSTITIAL PNEUMONIA (NSIP) – Fibrosing ILD

- An interstitial disease that does not fit into any other well-defined histologic pattern
- 25% of Idiopathic ILDs
- Seen in patients of both genders, **40-50 YEARS OLD –** *Middle age patients with milder symptoms than UIP!*
  - PROGNOSIS is better than UIP!
- **CLINICAL: GRADUAL** onset of dyspnea with a cough for several months
- **CHEST X-RAY: insensitive, WIDESPREAD opacities**
- **PATHOLOGY:**
  - Histologically, **all lesions at same stage of progression** with lymphocytes & some plasma cells
  - Mild, patchy or diffuse interstitial fibrosis
  - **NO fibroblastic foci & NO honeycombing**
  - Many eventually re-classified if it progresses into something else

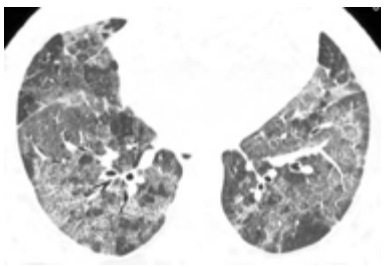
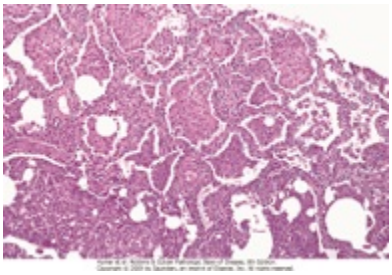
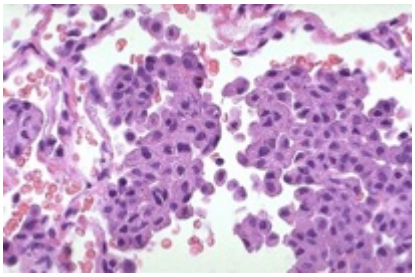
4. RESPIRATORY BRONCHIOLITIS-ASSOCIATED ILD (RB-ILD) – Smoking-related ILD

- Histologic lesion found in **CIGARETTE SMOKERS** characterized by **PIGMENTED INTRALUMINAL MACROPHAGES** within **1st & 2nd order RESPIRATORY BRONCHIOLES**
- 10% of Idiopathic ILDs
- Seen in **40-50 Y/O MALE SMOKERS**** *(30+ pack year history)*
- **CLINICAL**: **GRADUAL** onset of dyspnea with cough; usually mild
- **CHEST X-RAY**: thick peripheral bronchi
- **TREATMENT:** regresses with cessation of smoking



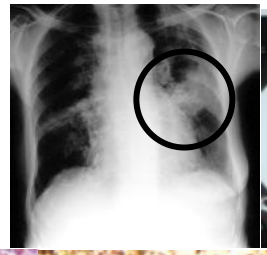
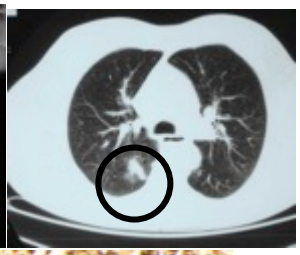
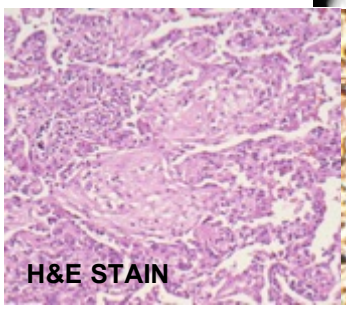
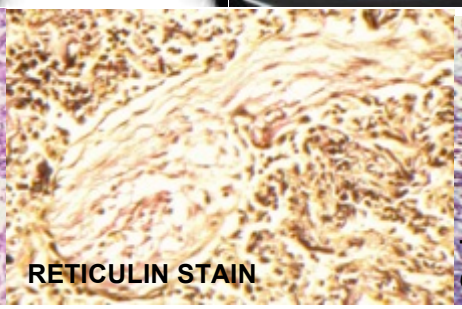
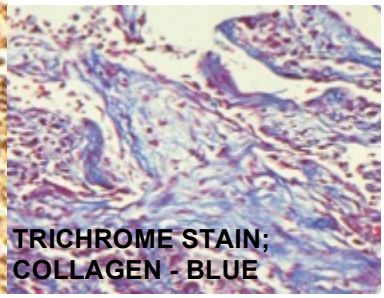
5. DESQUAMATIVE INTERSTITIAL PNEUMONIA (DIP) – Smoking-related ILD

- A disease characterized by the accumulation of large numbers of macrophages in alveoli with the majority of patients being SMOKERS
- 5% of Idiopathic ILDs
- Seen in **40-50 Y/O MALE SMOKERS****
- **CLINICAL**: **GRADUAL** onset of dyspnea with cough; often associated with **clubbing of digits**
- **CHEST X-RAY: insensitive, widespread opacities**
- **PATHOLOGY**: **MACROPHAGES** in the **ALVEOLI**, **minimal fibrosis**, NOT a UIP precursor
- **TREATMENT:** steroids & smoking cessation

6. CRYPTOGENIC ORGANIZING PNEUMONIA (COP) – Fibrosing ILD

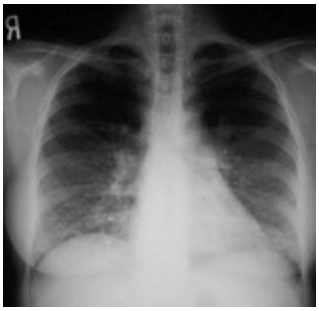
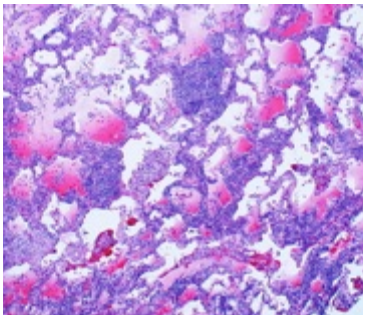
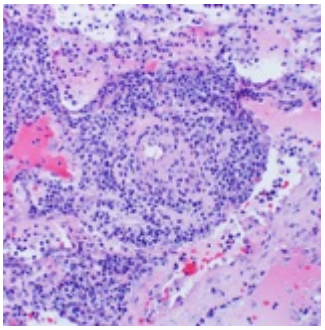
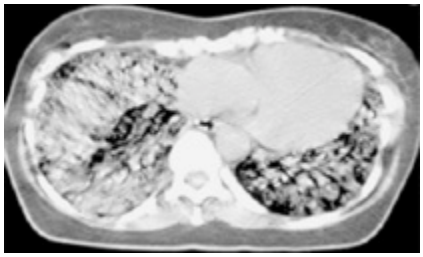
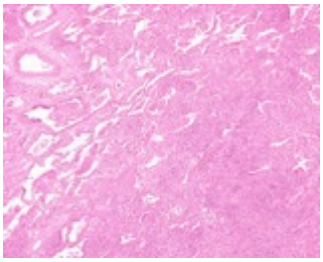
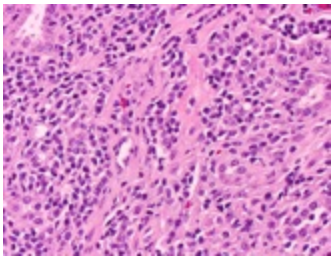
- AKA **Bronchiolitis Obliterans**
- Organization (new connective tissue) in **alveolar ducts & alveoli**
- 3% of Idiopathic ILD
- Seen in **55 Y/O PATIENTS**
- **CLINICAL**: **RECENT** onset of dyspnea & cough
- **CHEST X-RAY**: Focal areas of consolidation
- **PATHOLOGY**: tufts of organizing pneumonia in which all CT is of the **same age**; *no interstitial fibrosis*; characterized by present of **Polypoid plugs of LCT** (**MASSON BODIES**)
- **TREATMENT**: steroids

H&E STAIN | RETICULIN STAIN | TRICHROME STAIN; COLLAGEN - BLUE

7. LYMPHOCYTIC INTERSTITIAL PNEUMONIA (LIP)

- Syndrome of **fever**, cough, & dyspnea with **BIBASILAR** pulmonary infiltrates composed of **dense** interstitial accumulations of **lymphocytes & plasma cells**
- 1% of Idiopathic ILDs
- *Age & gender of patients is variable* *(BUT autoimmune diseases are more common in Women)*
- **ETIOLOGY:** associated with autoimmune & lymphoproliferation disorders – Rheumatoid Arthritis, Hashimoto Thyroiditis, allogenic bone barrow transplant, lupus & lymphoma, **HIV** type I, Epstein-Barr virus, & human T-cell leukemia virus (HTLV) type I
- **TREATMENT:** treat underlying disease; steroids; if not responsive to steroids, use alkylating agent
- **CHEST X-RAY**: bilateral, **LOWER ZONE**, reticular or reticulonodual opacities

AUTOIMMUNE DISEASES ASSOCIATED W/ ILD

Systemic Lupus Erythematosus, Rheumatoid Arthritis, Progressive Systemic Sclerosis, Dermatomyositis/Polymyositis

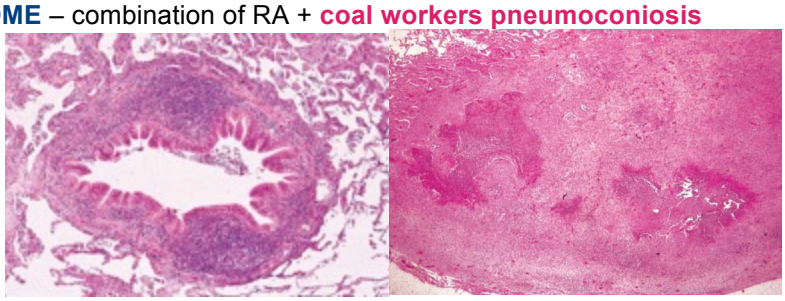
COMMON PATTERNS OF PULMONARY INVOLVEMENT

- Non-specific interstitial pneumonia
- Usual interstitial pneumonia
- Organizing pneumonia
- Bronchiolitis
- Vascular sclerosis

RHEUMATOID ARTHRITIS-RELATED LUNG DISEASE: Caplan Syndrome

- **CAPLAN SYNDROME** – combination of RA + **coal workers pneumoconiosis**

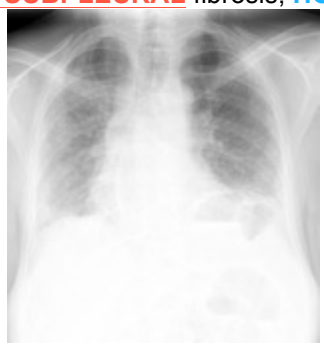
FOLLICULAR BRONCHIOLITIS

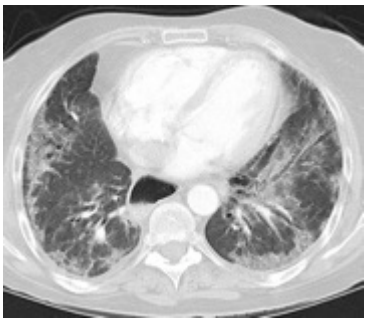


RHEUMATIC NODULE

PULMONARY FIBROSIS IN SCLERODERMA

- CXR not sensitive for diagnosis
- Diagnosis based on HRCT
  - 90% of patients
  - **BASILAR & SUBPLEURAL** fibrosis, **HONEYCOMBING**, **GROUNDGLASS** OPACITIES

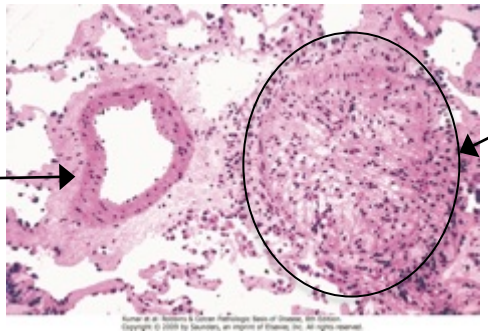




LUNG TRANSPLANTS – Treatment for ILD

- INDICATIONS: End stage lung disease
  - Idiopathic pulmonary fibrosis (UIP)
  - Emphysema
  - Cystic Fibrosis
  - Idiopathic/familial pulmonary HTN
- COMPLICATIONS
  - Infections – immunocompromised
  - Acute rejection (mononuclear with few PMNs & eosinophils)
  - Chronic rejection (bronchiolitis obliterans)
- Survivals: 78% at 1 year, 50% at 5 years, 26% at 10 years

Pulmonary artery branch is normal →



Total occlusion of bronchiole
BRONCHIOLITIS OBLITERANS

PULMONARY VALVULAR DISEASES

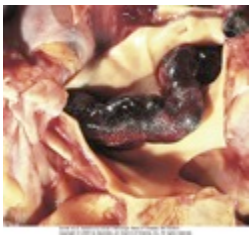
Pulmonary Embolism, Hemorrhage, & Infarction; Pulmonary HTN, Diffuse Pulmonary Hemorrhage Syndromes – Goodpasture Syndrome, Idiopathic Pulmonary Hemosiderosis, Polyangiitis with Granulomatosis (Wegener's)

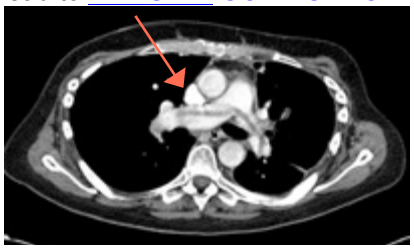
1. PULMONARY THROMBOEMBOLISM

- Small or large blood clot usually from the **deep veins of the LEG** *(not saphenous or any superficial veins!)*
- PE (pulmonary embolism) is a complication principally from patients who are already suffering from some underlying disorder:

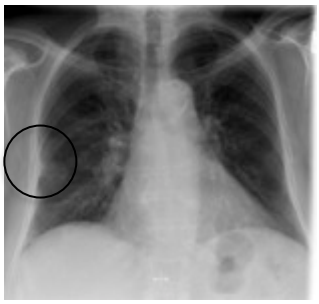
COMMON	PRIMARY HYPERCOAGULABLE STATE	SECONDARY HYPERCOAGULABLE STATE
IMMOBILIZATION **HIP FRACTURE** **CARDIAC DISEASE**	Factor V Leiden Prothrombin Mutation Antiphospolipid Syndrome	Obesity; Recent surgery; Cancer; Oral contraceptives; Pregnancy

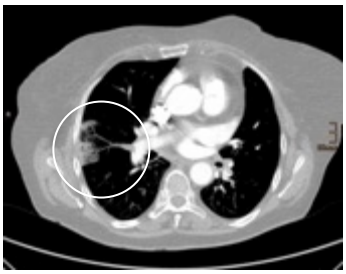
- **2 main consequences:** respiratory compromise (non-perfused segment) & hemodynamic compromise (increased resistance to pulmonary blood flow)
- **LARGE EMBOLI**
  - Lodges in the MAIN PULMONARY ARTERY or major branches or at bifurcation-**SADDLE EMBOLUS**
    - **+HOMAN'S SIGN**: pain in the calf on forceful & abrupt dorsiflexion of the patient's foot at the ankle while the knee is extended
  - *Dyspnea, shock, fever, & increase in serum LDH; electromechanical dissociation (heart is pumping, but blood flow is blocked – EKG will show sinus rhythm, but there are no palpable pulses!)*
  - May can **SUDDEN DEATH (10%)** or **ACUTE** COR PULMONALE **(leads to RV dilation!)**
    - *A large PE is one of the few causes of virtually instantaneous death*
- **SMALL EMBOLI**
  - Travels out into the more PERIPHERAL vessels
  - *Transient CP & cough* → **HEMORRHAGE**
  - *Dyspnea, tachypnea, fever, CP, cough, & hemoptysis* → **WEDGE-SHAPED INFARCT**
  - May lead to **CHRONIC** COR PULMONALE **(leads to RV hypertrophy!)**



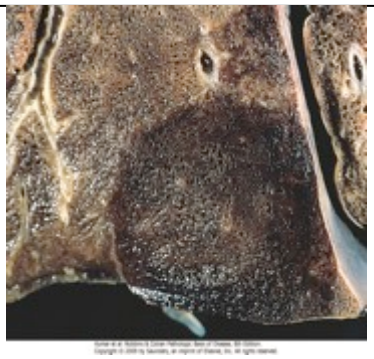


LARGE SADDLE EMBOLUS (**Friable, dark, well formed)* from the femoral vein lying aside the MAIN L & R PULMONARY A.

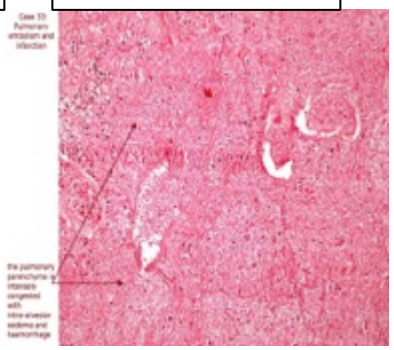


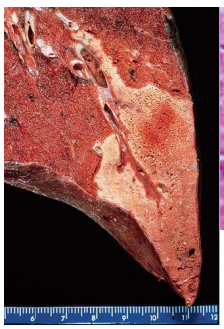


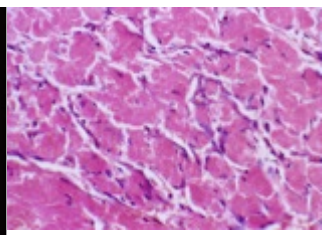
RECENT, ROUGHLY WEDGE-SHAPED HEMORRHAGIC PULMONARY INFARCT
Pt would probably present with hemoptysis



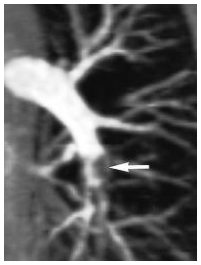
COAG. NECROSIS
Outline of infarcted alveoli
Alveoli filled with RBCs



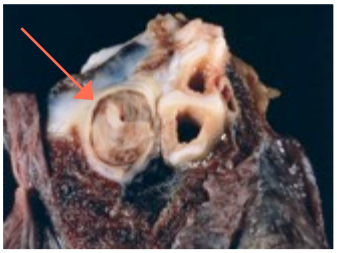




OLDER PULMONARY INFARCTION

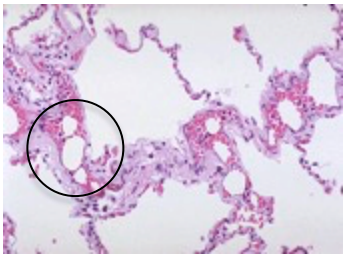
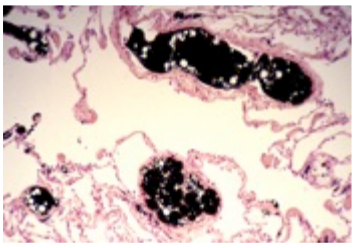


PE ANGIOGRAM

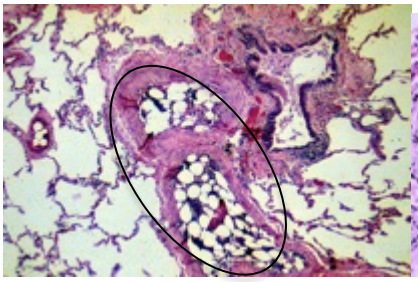
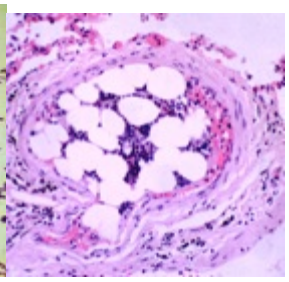


PE GROSS

OTHER FORMS OF EMBOLI

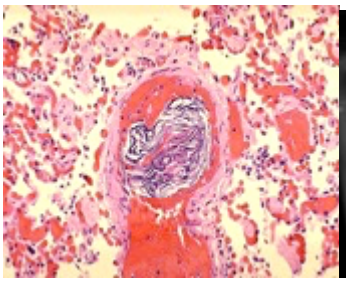
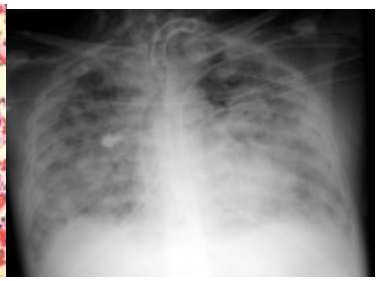



FAT EMBOLISM & SUDAN BLACK STAIN FRESH TISSUE

BONE MARROW EMBOLISM POST-CPR

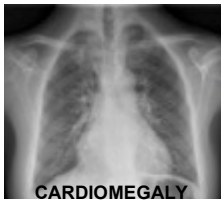
NORMAL

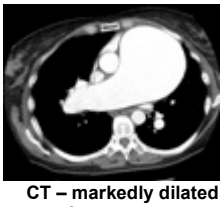
AMNIOTIC FLUID EMBOLISM

2. PULMONARY HYPERTENSION

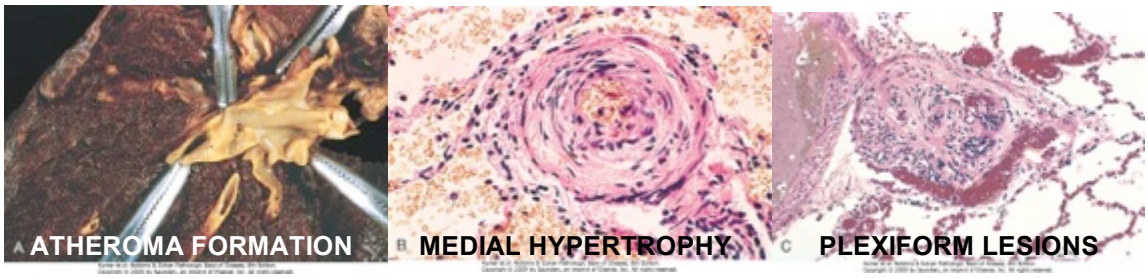
- Pulmonary HTN occurs when mean pulmonary pressure reaches ¼ of systemic levels
  - *Resting mean pulmonary arterial pressure of 25 mmHg or greater at R heart catheterization*
- Most common in **FEMALES 20-40 YEARS OLD**
- **Risk factors:** drugs & toxins; HIV; portal HTN & liver disease; CT disease
- PRIMARY PULMONARY VASCULAR SCLEROSIS – **YOUNG FEMALES**
  - Most often sporadic/idiopathic (94%)
  - AD inheritance pattern of BMPR2 mutation → pulmonary vascular thickening & occlusion → Primary HTN
- SECONDARY PULMONARY HTN
  - **COPD**, congenital & acquired heart disease, recurrent thromboembolization, systemic sclerosis, fenfluramine & phentermine (**DIETING PILLS**)
- **CLINICAL**: dyspnea; elevated R heart pressures; peripheral edema
  - **RIGHT SIDED HEART FAILURE**
    - Pleural effusion, JVD, congestion of spleen & kidney, **nutmeg liver** (chronic passive congestion)
    - **PERIPHERAL EDEMA;** NOT PULMONARY EDEMA!
    - **COR PULMONALE** – pure right sided heart failure secondary to pulmonary vascular HTN, as the result of primary vessel disease or diffuse lung disease
  - RIGHT VENTRICULAR HYPERTROPHY (Thickened wall – Concentric)
- **MORPHOLOGY**
  - LARGE VESSELS – changes simulating systemic atherosclerosis **(atheromatous deposits)**
  - SMALL VESSELS – medial hypertrophy (thick vascular wall), intimal fibrosis
    - Plexogenic pulmonary anteriopathy (primary HTN)
- **IMAGING**:
  - Elevated cardiac apex due to RV hypertrophy
  - Enlarged R atrium (Dilated – Eccentric)
  - Prominent pulmonary outflow tract
  - Enlarged pulmonary arteries
  - Pruning of peripheral pulmonary vessels



CARDIOMEGALY
Right Atrial Enlargement



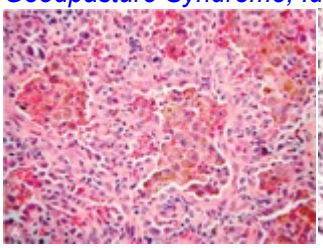
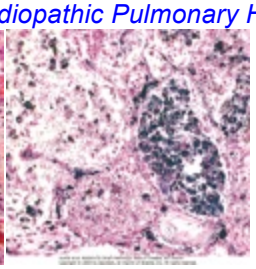
CT – markedly dilated pulmonary artery



RIGHT VENTRICULAR HYPERTROPHY
R ventricular wall is almost as thick as the L

3. DIFFUSE ALVEOLAR HEMORRHAGE SYNDROMES

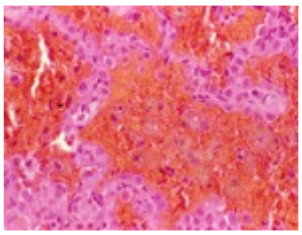
Goodpasture Syndrome, Idiopathic Pulmonary Hemosiderosis, Vasculitis (Wegener's, Hypersensitivity pneumonia, Lupus)

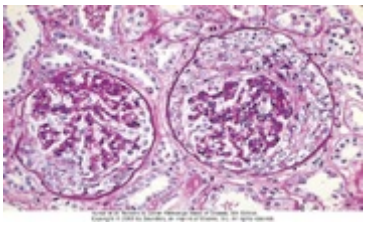



DIFFUSE PULMONARY HEMORRHAGE SYNDROME
Acute intra-alveolar hemorrhage & hemosiderin-laden macrophages, reflecting previous hemorrhage, are common features.
Prussian blue stain for iron.

GOODPASTURE SYNDROME

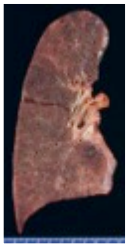
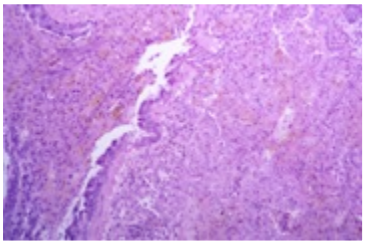
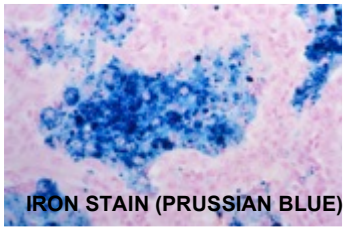
- Autoimmune disease most often involving the upper respiratory tract and/or the lung, with **HEMOPTYSIS** being the common presenting symptoms
- Most common in **YOUNG MALE SMOKERS****
- **LINEAR anti-glomerular basement membrane antibodies-α3 chain of collagen IV (AGBMA)**
- Trigger that exposes the Ag is unknown – smoking, virus, chemicals?
- Proliferative Rapidly Progressive Glomerulonephritis & Necrotizing Hemorrhagic Interstitial Pneumonitis
- RENAL FAILURE (UREMIA) is the most common cause of death
- **DIAGNOSTICALLY IMPORTANT FEATURES**
  - **CAPILLARITIS**
  - **SCATTERED, POORLY FORMED GRANULOMAS** *(unlike those of sarcoidosis, which are rounded & well defined!)*





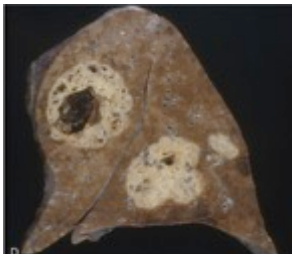
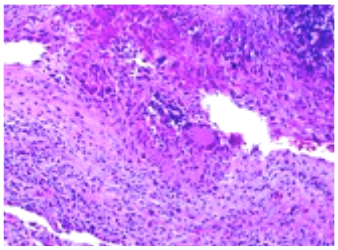
IDIOPATHIC PULMONARY HEMOSIDEROSIS

- RARE condition usually of **CHILDREN**
- Episodes of diffuse hemorrhage
- No antivascular anitbodies have been found, but immunosuppression works for treatment!
- **DIFFUSE HEMOSIDERIN DEPOSITION IN MACROPHAGES & ALVEOLAR WALLS**
- *Productive cough, hemoptysis, anemia, weight loss*

WEGENER GRANULOMATOSIS

- Commonly seen in **MALES in the 5th DECADE**, immunocompromised, variable prognosis
- NECROTIZING GRANULOMATOUS ARTERITIS of the lungs
- Capillaritis – *vasculitis*
- **NECROTIZING INFLAMMATION OF UPPER RESPIRATORY TRACT**
- Necrotizing Glomerulonephritis
- Subtle signs on transbronchial biopsy
- **CYTOPLASMIC PATTERN ANTI-NEUTROPHIL ANTIBODIES** (PR3/c-ANCA) in 85%

PULMONARY EOSINOPHILIA & ALVEOLAR PROTEINOSIS

PULMONARY EOSINOPHILIA

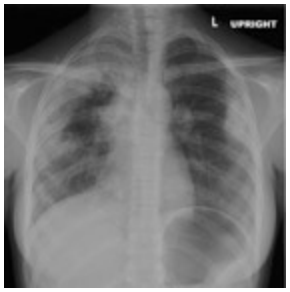
- 3 syndromes of pulmonary eosinophilia & blood eosinophilia
  - **ACUTE** eosinophilic pneumonia w/ respiratory failure
  - **SECONDARY** eosinophilia – *parasitic, fungal, & bacterial infections; hypersensitivity pneumonitis, drug allergies, asthma, allergic bronchopulmonary aspergillosis, vasculitis (Chur Strauss)*
  - **CHRONIC** (idiopathic) eosinophilic pneumonia

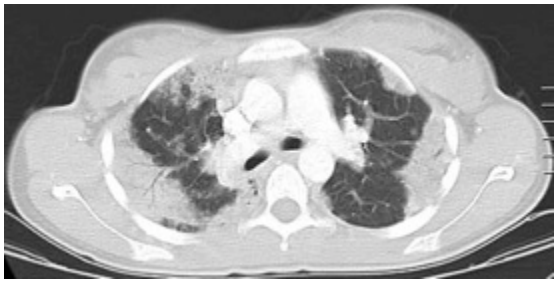
ACUTE EOSINOPHILIC PNEUMONIA W/ RESPIRATORY FAILURE

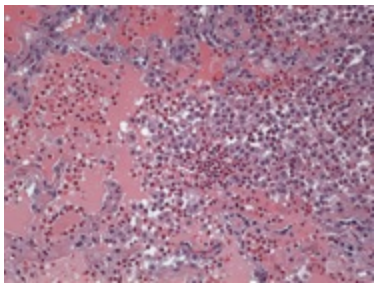
- An acute illness of unknown etiology
- **CLINICAL:** rapid onset with fever, dyspnea, & hypoxemic respiratory failure
- **CHEST X-RAY**: diffuse infiltrates
- **LAB**: bronchoalveolar lavage fluid >25% eosinophils; blood eosinophilia
- **PATHOLOGY**: **diffuse alveolar damage with eosinophils**
- **TREATMENT**: corticosteroids

IDIOPATHIC CHRONIC EOSINOPHILIC PNEUMONIA

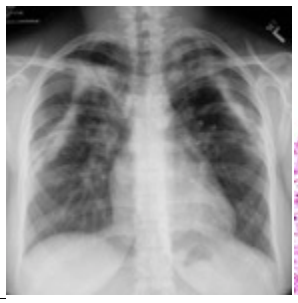
- Focal areas of cellular consolidation of the lung substance distributed chiefly in the **PERIPHERY** of lung fields
- **CLINICAL:** cough, fever, night sweats, dyspnea, & weight loss
- **CHEST X-RAY**: homogeneous peripheral airspace consolidation, reverse pulmonary edema
- **LAB**: bronchoalveolar lavage fluid >25% eosinophils; blood eosinophilia
- **PATHOLOGY**: **heavy aggregates of lymphocytes & eosinophils within both the SEPTAL WALLS & ALVEOLAR SPACES; interstitial fibrosis & organizing pneumonia are often present**
- **TREATMENT**: corticosteroids

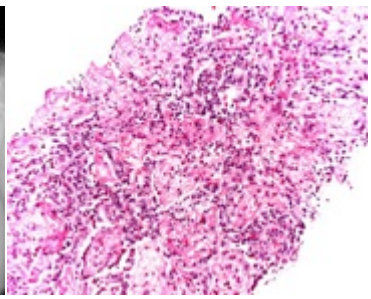






Intraalveolar eosinophils & HISTIOCYTES

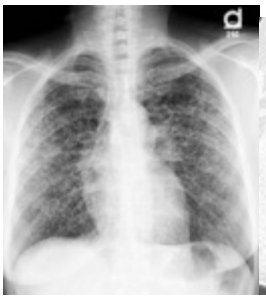


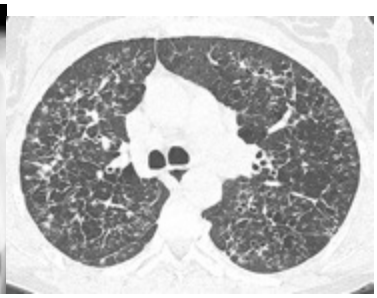


CHRONIC EOSINOPHILIC PNEUMONIA
Case: 24 y/o female patient with history of asthma & intermittent fever

PULMONARY LANGERHANS CELL HISTIOCYTOSIS

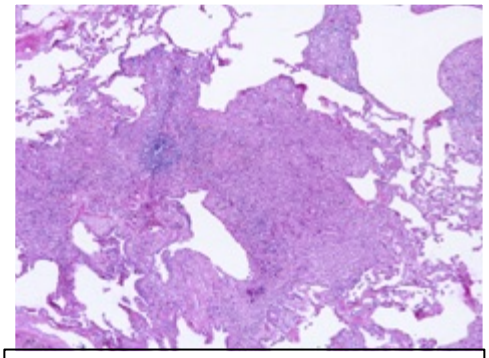
- Proliferations of a special type of immature dendritic cell called the Langerhans cell
- Most common in **ADULT SMOKERS****
- **ETIOLOGY:** thought to be reactive, but 40% have **BRAF** mutation, which is found in other forms; *likely neoplastic*
- **PATHOLOGY**: proliferation of Langerhans cells with eosinophils; monocyte-macrophage lineage & act as APCs
- **IMMUNOSTAINS:** S100, CD1a
- **EM: BIRBECK GRANULES** – *tennis-racket shaped with central linear density*
- PROGNOSIS: improve after they stop smoking, but can develop focal fibrosis resulting in restrictive lung disease



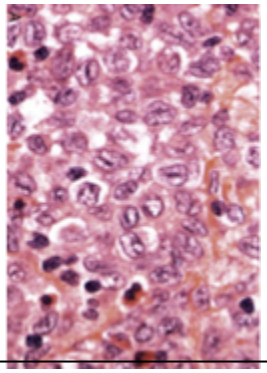


PULMONARY LANGERHANS CELL HISTIOCYTOSIS
46 y/o African American female with progressive dyspnea; occasional non-purulent cough; smoker w/ obstruction on pulmonary function test

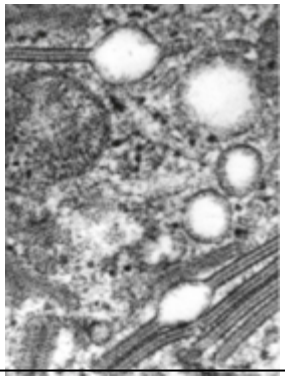
Ill-defined or stellate nodules
Reticulonodual infiltrates – UPPER to MID-lung zone
Upper zone cysts
Preservation of lung volumes



H&E – low power with infiltration



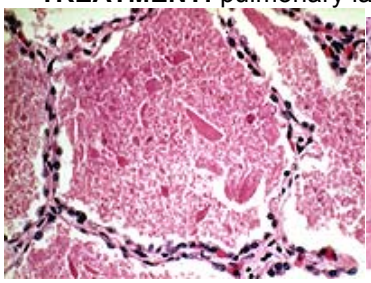
LANGERHANS CELLS

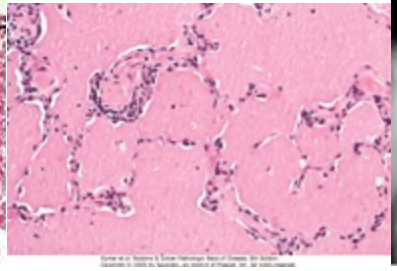


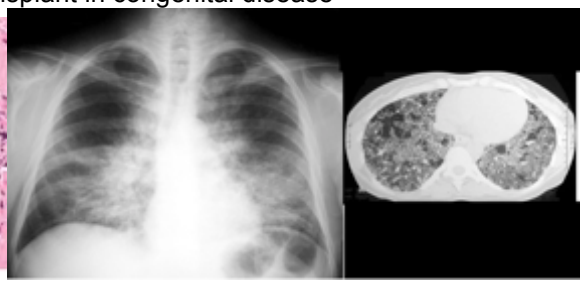
EM: BIRBECK GRANULES

PULMONARY ALVEOLAR PROTEINOSIS

- Rare disease caused by defects related to granulocyte-macrophage colony-stimulating factor (GM-CSF) or **pulmonary macrophage dysfunction** resulting in the accumulation of surfactant in the intra-alveolar & bronchial spaces
- 3 TYPES:
  - **AUTOIMMUNE** (Acquired) – **90% of cases**; **20-50 y/o ADULTS**; variable course with an Ab to GM-CSF
    - *Loss of GM-CSF signaling blocks the terminal differentiation of alveolar macrophages impairing their ability to catabolize surfactant*
  - **SECONDARY** – rare; many lung disorders such as acute silicosis, immunodeficiency syndrome, malignancy, blood disorders which impair macrophages
  - **HEREDITARY** – rare; genetic with a loss of GM-CSF signaling; fatal
- **CLINICAL**: uncommon, cough & sputum with gelatinous chunks
- **CHEST X-RAY**: bilateral, patchy distribution; **predominantly PERI-HILAR & LOWER LOBE** consolidations
- **CT***:* GROUND-GLASS OPACITIES
- **PATHOLOGY***:* accumulation of acellular surfactant in the intra-alveolar & bronchiolar spaces;
  - **Risk for NOCARDIA & MYCOBACTERIAL INFECTIONS**
- **TREATMENT:** pulmonary lavage & GM-CSF therapy or transplant in congenital disease

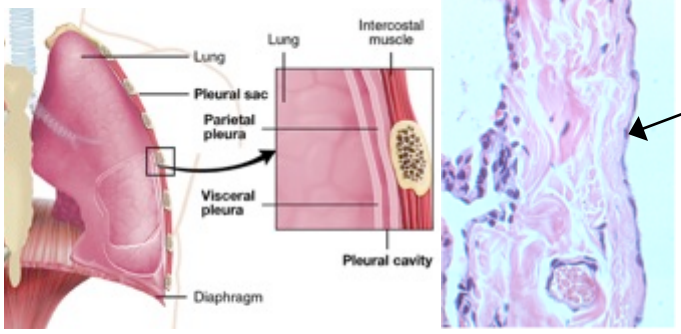






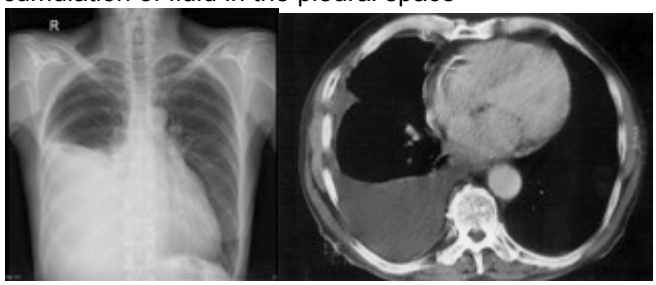
PLEURAL & MEDIASTINAL DISEASES

PLEURA: pair of serous membranes lining the thorax & enveloping the lungs



Pleural mesothelial cells

PLEURAL EFFUSION: accumulation of fluid in the pleural space



TRANSUDATE: extracellular fluid with a LOW protein, LOW specific gravity, & LOW cell count
- *Clear, few RBCs, many lymphocytes*

EXUDATE: a mass of cells & fluid that has seeped out of blood vessels or an organ, especially in inflammation
- *Usually cloudy, HIGH protein, HIGH WBCs, many neutrophils*
- ↑ Hydrostatic pressure – CHF
- ↑ Vascular permeability – Pneumonia
- ↓ Osmotic pressure – Nephrotic Syndrome
- ↑ Intrapleural negative pressure – Atelectasis
- ↓ Lymphatic drainage – Mediastinal carcinomatosis (lymphatic obstruction)

INFLAMMATORY PLEURAL EFFUSIONS

- **EMPYEMA**: purulent pleural exudate due to bacterial or mycotic seeding loculated, yellow-green, creamy pus composed of masses of neutrophils
- **HEMORRHAGIC PLEURITIS**: sanguineous inflammatory exudates seen in hemorrhagic diatheses, rickettsial diseases, & neoplastic involvement of the pleural cavity

NON-INFLAMMATORY PLEURAL EFFUSIONS

- **HYDROTHORAX**: collections of serous fluid within the pleural cavities; increased hydrostatic pressure – CHF
- **CHYLOTHORAX**: milky fluid, usually of lymphatic origin

PULMONARY INFECTIONS

Pneumonia, Pulmonary Abscess, Tuberculosis

PNEUMONIA

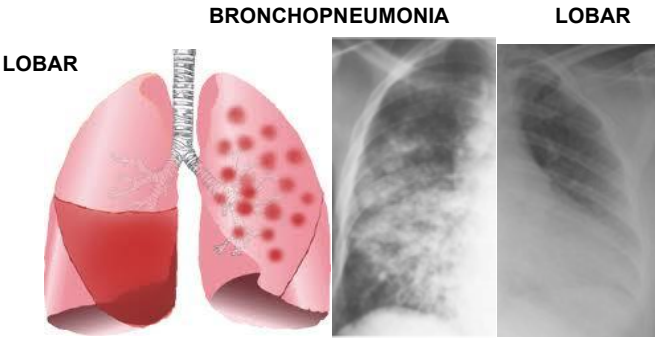
- Broadly defined as any infection (bacterial, viral, mycoplasmal, fungal) of the lung parenchyma (can also be chemical or radiation)
- RESPIRATORY TRACT involved in infections more than any other organ system
- 8th leading cause of death in the US
  - Mortality is highest for community acquired pneumonia (CAP) who require hospitalization
- Common in **ADULTS >5th DECADE** & who have some **CO-MORBIDITY** (COPD, cardiovascular, or other chronic disease)
- **PRE-DISPOSING CONDITIONS: LOSS OF ANY HOST DEFENSE**
  - *Loss of normal cough reflex, injury to mucociliary apparatus, accumulation of secretions, edema & congestion, abnormalities of phagocytosis or bactericidal activities, splenectomy (encapsulated pneumococcus)*

THE PNEUMONIA SYNDROMES

- **COMMUNITY-ACQUIRED ACUTE PNEUMONIA** (alveolar exudates or interstitial infiltrates)
  - *Strep. Pneumoniae; H. influenza; S. aureus; M. pneumoniae; viruses*
- **HEATH CARE ASSOCIATED PNEUMONIA**
  - *S. aureus* methicillin resistant; *P. aeruginosa*
- **HOSPITAL-ACQUIRED (NOSOCOMIAL) PNEUMONIA**
  - Gram negative rods (*Klebsiella; S. marcescens; E. coli*)
- **ASPIRATION PNEUMONIA**
  - Anaerobic (*Bacteroides*) & Aerobic (*S. aureus*)
  - **Alcoholics, problems with gag reflex
- **CHRONIC PNEUMONIA**
  - Granulomatous (*M. tuberculosis,* Mycosis)
- **NECROTIZING PNEUMONIA & LUNG ABSCESSES**
  - *Staph aureus*
  - Anaerobic bacteria with or without mixed aerobic infection
  - **Bronchiectasis
- **PNEUMONIA IN THE IMMUNOCOMPROMISED HOST**
  - Cytomegalovirus; *Pneumocystic jiroveci; M. avium-intracellulare*

1. BACTERIAL PNEUMONIA: Bronchopneumonia & Lobar Pneumonia

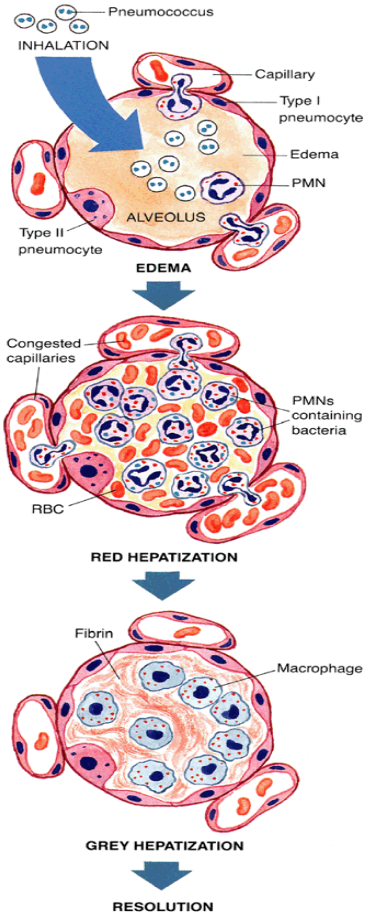
- Usually in **OLDER patients**
- **CAP ACUTE bacterial pneumonia** usually onset with **abrupt** high fever, shaking chills, & cough with mucopurulent sputum; possible hemoptysis
- **CHEST X-RAY**: airspace opacity, **LOBAR** consolidation, or interstitial opacity
  - **LOBAR CXR**: ENTIRE LOBE consolidated & air bronchograms common
  - **BRONCHOPNEUMONIA CXR**: multifocal, **PATCHY** infiltrates, & sometimes without air bronchograms
- **TREATMENT:** take cultures, start appropriate abx, identify organism, test for sensitivity, focused abx
- **COMPLICATIONS:** tissue destruction & necrosis → abscess, empyema, meningitis, endocarditis, or pericarditis



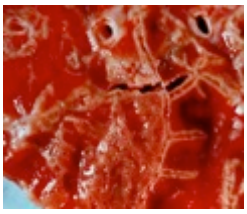
Air bronchogram: phenomenon where air-filled bronchi (dark) are made visible by the opacification of surrounding alveoli (grey/white).

LOBAR PNEUMONIA

- CLASSIC PNEUMOCOCCAL PNEUMONIA
- **PATHOLOGY: 4 STAGES**
  - **CONGESTION** – the lung is heavy, boggy, & red; characterized by vascular engorgement, intra-alveolar fluid w/ few neutrophils, & often present of numerous bacteria
  - **RED HEPATIZATION** – characterized by massive confluence exudation, as neutrophils, RBCs, & fibrin fill the alveolar spaces; gross examination, lobe appears distinctly red, firm, & airless, with a liver-like consistency
  - **GRAY HEPATIZATION** – progressive disintegration of RBCs & the persistence of a fibrinosuppurative exudate, giving the gross appearance of a grayish-brown, dry surface
  - **RESOLUTION** – exudate within the alveolar spaces is broken down to produce granular, semifluid debris that is resorbed, ingested by macrophages, expectorated, or organized by fibroblasts growing into it



RED HEPATIZATION

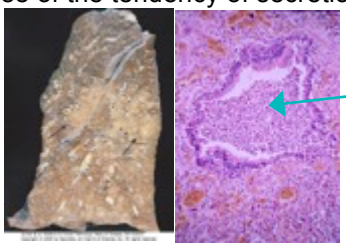


GRAY HEPATIZATION

BRONCHOPNEUMONIA (LOBULAR)

- Often *Staphylococcus*
- **PATHOLOGY**
  - Multiple consolidated areas of acute suppurative inflammation
  - Consolidation may be **PATCHY** through one lobe, but is more often **MULTILOBAR** & frequently **BILATERAL & BASAL** because of the tendency of secretions to gravitate to the LOWER LOBES

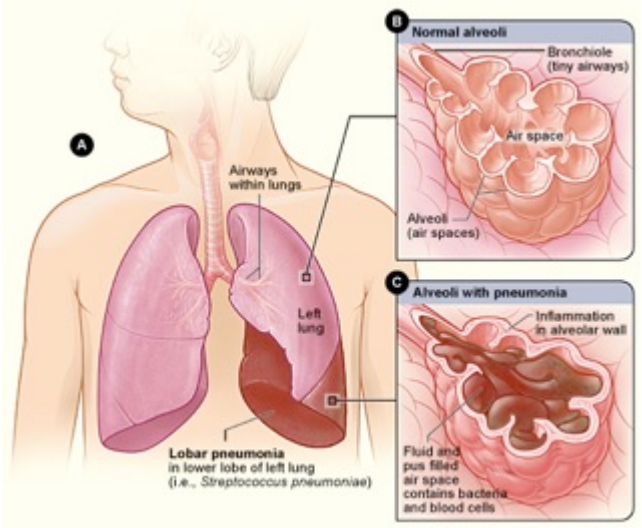
BRONCHOPNEUMONIA
Patches of consolidation (arrows)

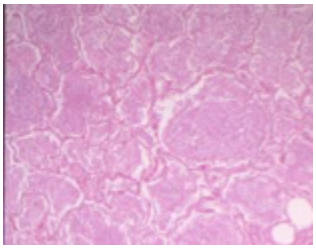


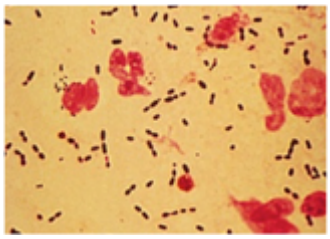
BRONCHOPNEUMONIA
Bronchiole filled with neutrophils

***STREPTOCOCCUS PNEUMONIAE* – Most Common Typical/Acute Community Acquired Pneumonia**

- *Gram positive, lancet shaped diplococci*
- 95% of **LOBAR PNEUMONIA**
- Bacterial invasion of the lung parenchyma causing alveoli to be filled with intra-alveolar polymorphonuclear **inflammatory exudate** (high protein, high neutrophils)
- **PREDISPOSING CONDITIONS** – **Elderly**, chronic disease (CHF, COPD, DM), congenital or acquired immune deficiency or absent of splenic function (encapsulated organisms)
- Presents with **production cough** of rusty sputum
- **EXAMINATION**: dullness on percussion, decreased breath sounds, consolidated lung on CXR

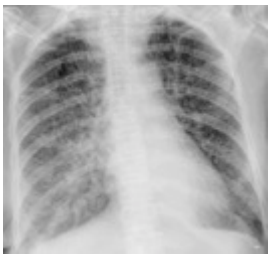


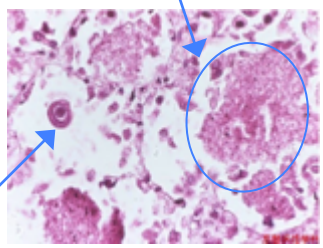




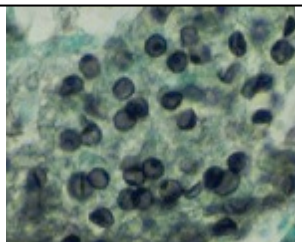
2. VIRAL/ATYPICAL PNEUMONIAS – CAP of Immunocompromised Host

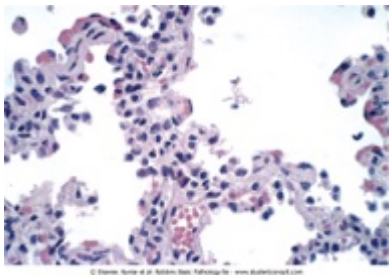
- Viral: self-limited "chest cold," but based on the patient & organism can be lethal
  - Secondary bacterial infection is often lethal
- "INTERSTITIAL PNEUMONIAS" are classically viral pneumonia & mycoplasma pneumonia, but can also be HIV pneumocystis pneumonia



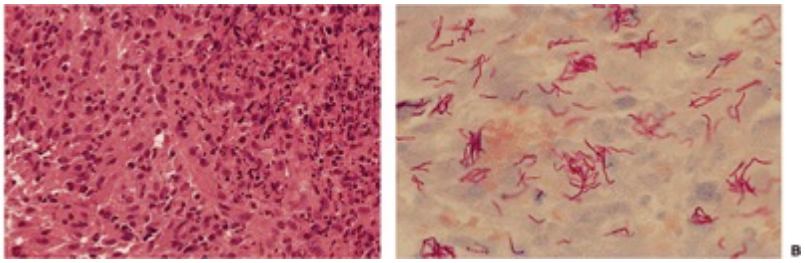


Pneumocystis – Silver Stain





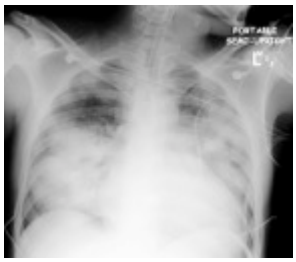
ATYPICAL PNEUMONIA
The thickened alveolar walls are heavily infiltrated with mononuclear leukocytes



***M. avium intercellulare* in an AIDS patient**
**Note lack of well-formed granulomata*

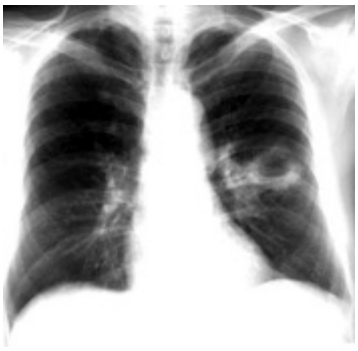
MYCOPLASMA PNEUMONIA

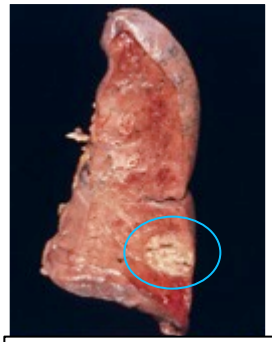
- ***Mycoplasma pneumonia is one of the most common causes of atypical pneumonia***
- Transmission person-to-person by infected respiratory droplets during close contact
- **CLINICAL**
  - EXTRAPULMONARY ABNORMALITIES (important & may suggest the diagnosis)
    - Hemolysis, skin rash, joint involvement, S/S indicative of GI tract, CNS, & heart disease
  - HEART – rhythm disturbances, CHF, CP, & conduction abnormalities on the ECG
- **CHEST X-RAY HAS 4 FREQUENTLY DESCRIBED PATTERNS:**
  - **Bronchopneumonia**
  - **Plate-like atelectasis**
  - **Nodular infiltration**
  - **Hilar adenopathy**

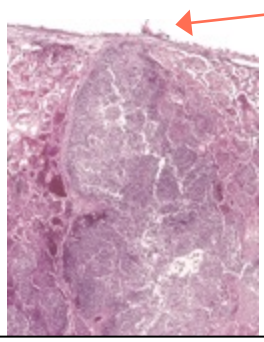


3. PULMONARY ABSCESSES

- An area of suppurative destruction of lung tissue usually caused by aerobic & anaerobic streptococci, *Staph aureus*, & a host of gram negative organisms
- Also caused by:
  - **ASPIRATION** of infective material (usually involves RIGHT lung) – ***most common cause***
    - Seen in ALCOHOLICS, coma patients, etc.
  - Septic embolism (thrombophlebitis or vegetations)
  - Neoplasms due to bronchial obstruction
    - *Neoplasms destroying parenchyma, neutrophils come in as 1st step of repair*
  - Miscellaneous: direct traumatic penetration
- **CLINICAL:** cough, copious amounts of **foul-smelling** (Anaerobes!) purulent or sanguineous sputum; fever, CP, weight loss
- **CHEST X-RAY: AIR-FLUID LINE!***
- **COMPLICATIONS:** extension to pleural cavity, hemorrhage, brain abscess, meningitis







PYEMIC LUNG ABSCESS with complete destruction of underlying parenchyma within the focus of involvement.

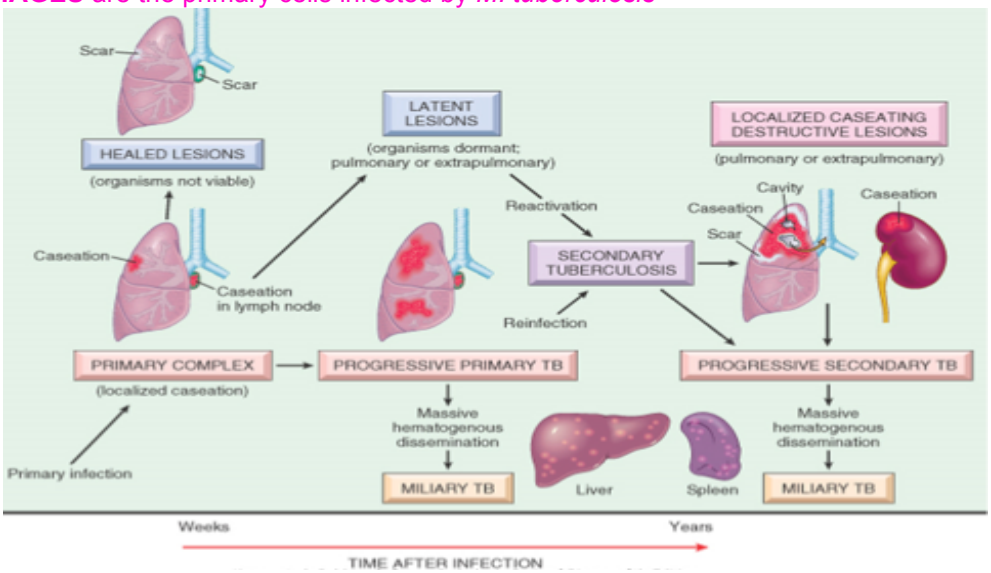
4. CHRONIC PNEUMONIAS – Granulomatous Pneumonia

Tuberculosis, Fungal or Mycotic Infections, Histoplasmosis, Blastomycosis, Coccidioidomycosis

- Frequently a localized lesion in **IMMUNOCOMPROMISED** patients

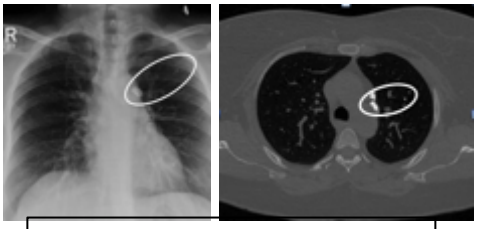
TUBERCULOSIS

- Disease of the **ELDERLY**, the **URBAN POOR**, & **AIDS PATIENTS**
- Disease states that increase risk: DM, Hodgkin Lymphoma, chronic lung disease (**Silicosis**), chronic renal failure, malnutrition, immunosuppression, & alcoholism
- **INFECTION:** presence of organisms, may or may not cause clinical symptoms
- **Delayed-type hypersensitivity → GRANULOMAS**
- *M. tuberculin* Ag detected by PPD – Positive PPD: cell-mediated immunity to tubercular Ag
- **MACROPHAGES** are the primary cells infected by *M. tuberculosis*

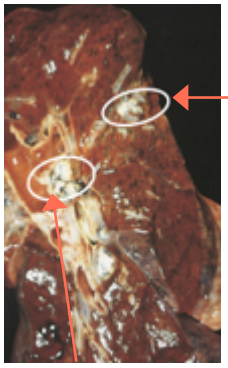


PRIMARY TUBERCULOSIS

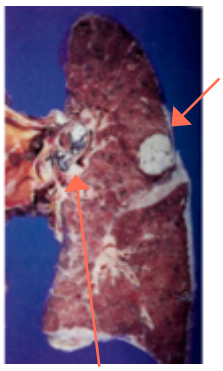
- Characterized by **GHON COMPLEX**
  - When Ghon complex heals & calcifies, it is called the **RANKE COMPLEX**
- **Peripheral, mid-lung** caseating lesion (Ghon focus) + enlarged, caseous **HILAR LYMPH NODES**
- Usually presents at **Early Age (Children)**
- *Usually asymptomatic*



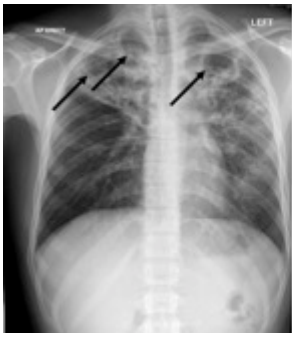
RANKE COMPLEX when the Gohn Complex is calcified

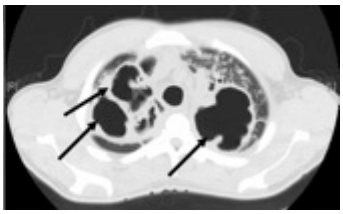


Draining hilar LN



Draining hilar LN

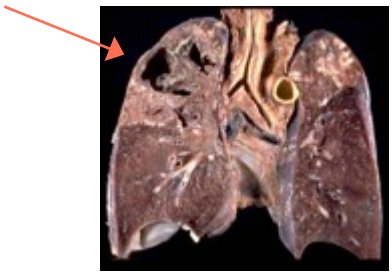




CAVITARY Post-Primary

SECONDARY TUBERCULOSIS

- Reactivation or re-infection
- **APICAL** **cavitary** lesions of one or both lungs – *because APEX IS MORE VENTILATED*
- Early caseation
- Fibrotic & calcified primary lesion
  - **Dystrophic calcification**



CAVITARY LESION IN THE APEX

NOTE: There are 3 Classical Apical Lesions in the Lung:

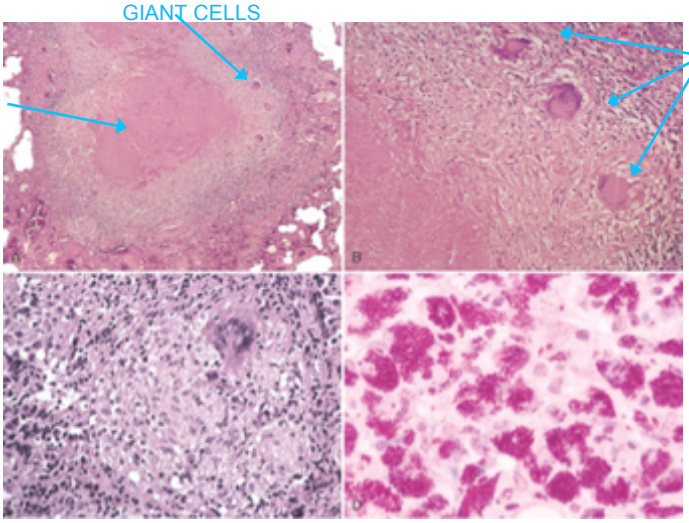
1. Cavitary, reactive TB (Secondary TB)
2. Aspergillus – Fungal ball in apex
3. Pancoast Tumor → SOLID MASS → Horner's Syndrome

TUBERCULOSIS – Histology

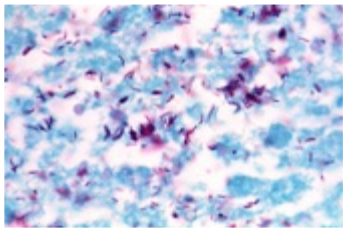
- Granuloma with central caseating necrosis surrounded by macrophages (epithelioid cells) & Langerhans type giant cells; the peripheral zone contains lymphocytes

GIANT CELLS

Eosinophilic center = CASEOUS NECROSIS
*No cell borders seen in caseating necrosis



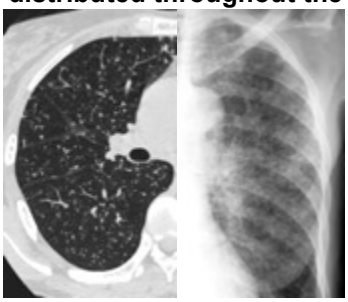
LANGERHANS GIANT CELLS
Nuclei are in a horseshoe-shaped pattern at the cell periphery!

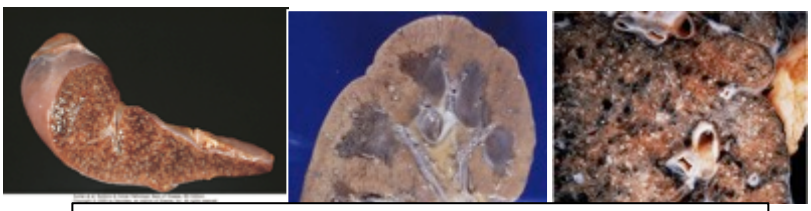


IMMUNOCOMPROMISED PTS
Macrophages packed with mycobacteria – Acid Fast Stain

MILIARY TUBERCULOSIS

- Form of tuberculosis that is characterized by a wide dissemination into the human body & by the tiny size of the lesions (1–5 mm). Its name comes from a distinctive pattern seen on a chest radiograph of many **TINY SPOTS distributed throughout the lung fields** with the appearance similar to **MILLET SEEDS**





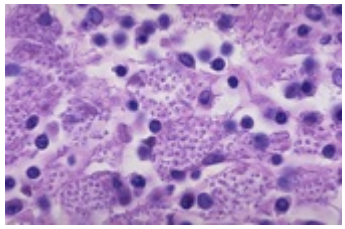
MILIARY TUBERCULOSIS OF THE SPLEEN, KIDNEY, & LUNG

*Histoplasmosis, blastomycosis, and coccidioidomycosis are discussed together because (1) they are **granulomatous diseases** of the lungs that may resemble tuberculosis, (2) they are caused by fungi that are thermally dimorphic in that they grow as hyphae that produce spores at environmental temperatures but grow as yeasts (spherules or ellipses) at body temperature within the lungs, and (3) each fungus is geographic in that it causes disease primarily among immunocompetent individuals living along the **Ohio and Mississippi rivers** & **Caribbean (Histoplasma)**, **central and SE US (Blastomyces)**, and **SW & West of the US and in Mexico (Coccidioides)**.*

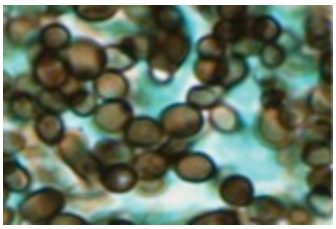
HISTOPLASMOSIS – *Histoplasmosis capsulatum*

- OHIO & MISSISSIPPI RIVER VALLEY & CARIBBEAN
- Soil-inhabitating dimorphic fungus; soil spores (microconidia & macroconidia) from BIRD & BAT FECES
- **TYPES: SELF-LIMITING; CHRONIC PROGRESSIVE; EXTRAPULMONARY; WIDELY DISSEMINATED**

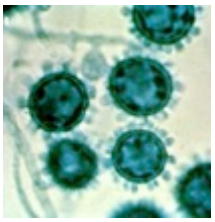
GRANULOMA of the lung



Organism in HISTIOCYTES
"Alveolar macrophages w/ intracellular yeast"

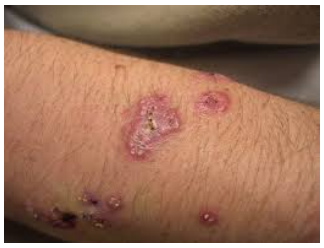


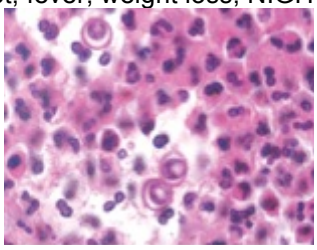
Pleomorphic, budding yeast



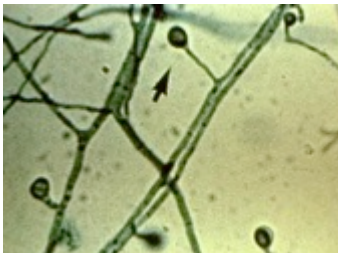
BLASTOMYCOSIS

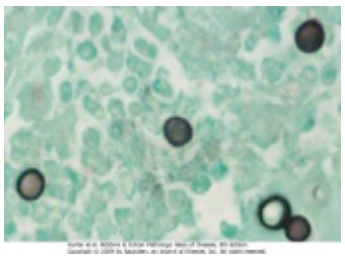
- CENTRAL & SE USA
- Soil spores (microconidia)
- Dimorphic fungus that causes systemic fungal infection
- **TYPES: PULMONARY; DISSEMINATED; PRIMARY CUTANEOUS FORMS**
- **CLINICAL**: abrupt onset, fever, weight loss, NIGHT SWEATS





Rounded budding yeast, larger than neutrophils

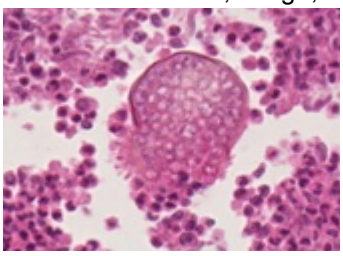




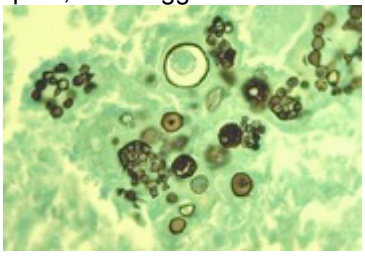
NOTE: **thick wall, nuclei, broad-based bud**

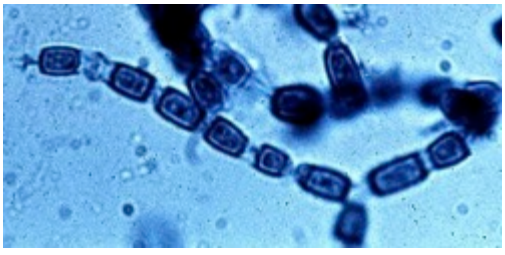
COCCIDIOIDOMYCOSIS

- SOUTHWEST & FAR WEST & MEXICO
- Soil spores (arthroconidia)
- **TYPES: ASYMPTOMATIC WITH LOCALIZED PULMONARY; DISSEMINATED**
- **CLINICAL:** fever, cough, chest pain; more aggressive in **FILIPINOS & AFRICAN AMERICANS**



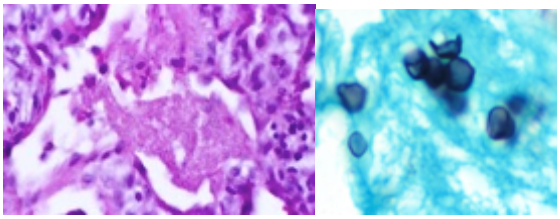
SPHERULES



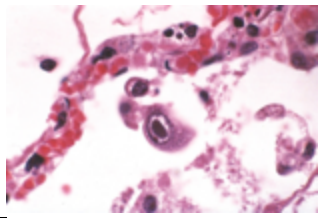


PULMONARY DISEASE IN IMMUNOCOMPROMISED HOST

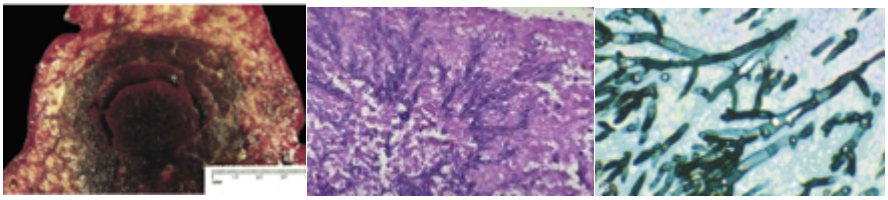
DIFFUSE INFILTRATE		FOCAL INFILTRATE	
COMMON	**UNCOMMON**	**COMMON**	**UNCOMMON**
Cytomegalovirus (CD4 <50) *Pneumocystis jiroveci* (<200) Drug reaction	Bacteria *Aspergillus* *Cryptococcus* Malignancy	Gram negative rods *Staphylococcus aureus* *Aspergillus* *Candida* Malignancy	*Cryptococcus* *Mucor* *Pneumocystis jiroveci* *Legionella pneumophilia*



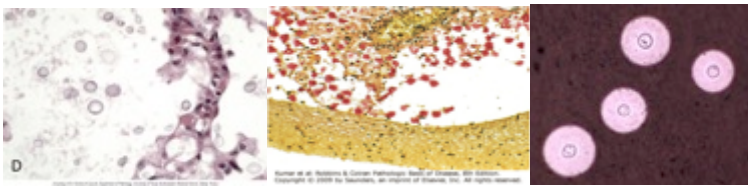
PNEUMOCYSTIS PNEUMONIA



CYTOMEGALOVIRUS: Distinct nuclear & ill-defined cytoplasmic & well-defined nuclear inclusions in the lung, known as **OWL'S EYE**

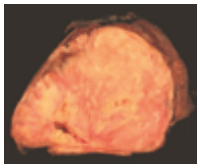


INVASIVE ASPERGILLOSIS:
Note septate hyphae with **acute-angle branching** in third image



CRYPTOCOCCUS
Lung of an AIDS patient; the yeast forms are somewhat variable in size

SOLITARY (LOCALIZED) FIBROUS TUMOR



- A rare mesenchymal tumor, probably from fibroblasts; it forms a tumor that hangs from the pleural
- CD34 +, Keratin –
- NAB2-STAT6 fusion gene

MEDIASTINAL TUMORS & OTHER MASSES		
ANTERIOR MEDIASTINUM	**POSTERIOR MEDIASTINUM**	**MIDDLE MEDIASTINUM**
Thyoma, Teratoma, Terrible Lymphoma Thyroid lesions, Parathyroid tumors Metastatic carcinoma	Neurogenic tumors (schwannoma, neurofibroma), Lymphoma Metastatic tumor (most from LUNG) Bronchogenic cyst Gastroenteric hernia	Bronchogenic cysts, Pericardal cyst, Lymphoma

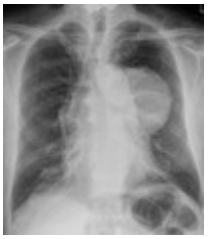
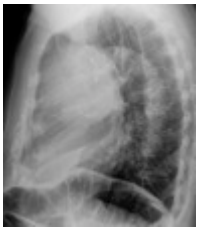
TUMORS OF ANTERIOR MEDIASTINUM (Bonus?)

ALL T's: Thyroid, Thyoma, Terrible lymphoma, Teratoma

MEDIASTINAL THYROID

- Usually occurs in **OLDER** patients
- **CLINICAL:** chest pain, cough, dyspnea, mediastinal compression (dysphagia, hoarseness, SVC Syndrome)
- **CT**: continuity of thyroid & medastinal lesion
- **TREATMENT:** resection, because malignancy may be present

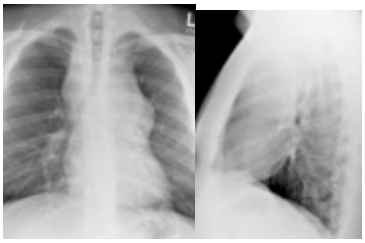
THYOMA

- 20-30% of anterior mediastinal tumors
- Overs in males or females **OVER 40**
- **CLINICAL**:
  - 40% - impingement on a mediastinal structure
  - 30-45% - detected in evaluation of **myasthenia gravis**
  - Other autoimmune – RBC aplasia, Grave's disease, pernicious anemia, Cushing's, other
- **PATHOLOGY**: biphasic tumor with epithelial cells & lymphocytes

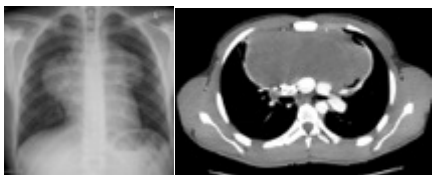
TERRIBLE LYMPHOMA

- 15% of anterior mediastinal masses
- Occurs in patients between **30-50**
- **CLINICAL**: chest pain, cough, dyspnea, mediastinal compression (dysphagia, hoarseness, SVC Syndrome)
- **PATHOLOGY**:
  - Nodular sclerosing Hodgkin Lymphoma (50-70%)
  - Lymphoblastic Lymphoma



TERATOMA or MALIGNANT GERM CELL TUMOR

- 15-20% of anterior mediastinal tumors; 50-60% benign
- Onset **20-30 years old**; usually benign, except the **MALES** get malignancy
- **CLINICAL:** chest pain, cough, dyspnea, mediastinal compression (dysphagia, hoarseness, SVC Syndrome)
- **PATHOLOGY OF 4 TYPES (SERUM MARKERS) OF MALIGNANT TERATOMAS:**
  - SEMINOMA – placental alkaline phostase (PLAP)
  - CHORIOCARCINOMA - β-human chorionic gonadotropic (β-hCG)
  - Yolk sac tumor - α-fetaprotein
  - Embyonal carcinoma

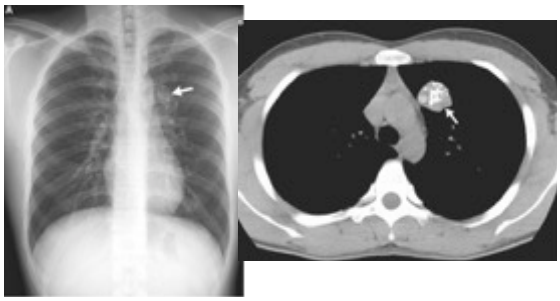
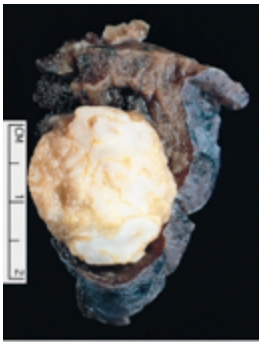
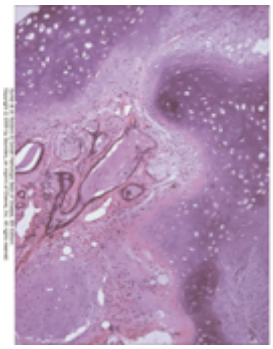


BENIGN LUNG NEOPLASMS

Pulmonary Hamartoma, Lymphangioleiomyomatosis (LAM), Inflammatory Myofibroblastic Tumor (IMT)

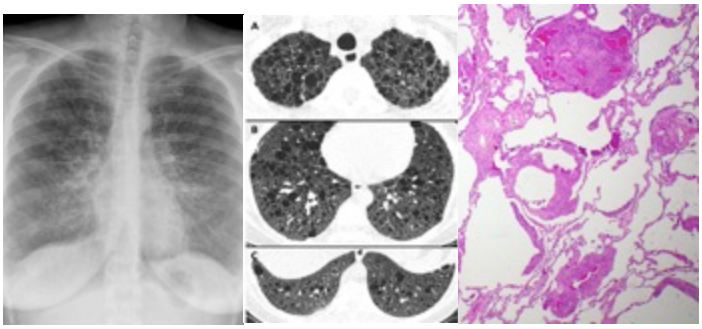
PULMONARY HAMARTOMA

- BENIGN neoplasm resembling the tissue of its origin – composed of cartilage, fat, & fibrous tissue, as well as entrapped respiratory epithelium
- Most often in **OLDER** patients
- **Generally asymptomatic; incidental finding with calcifications**
- **GROSS PATHOLOGY**: resembles **POPCORN**

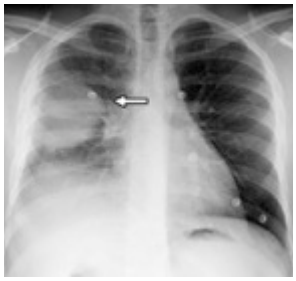
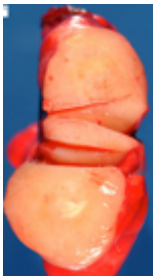
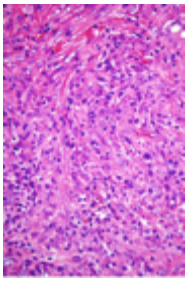
LYMPHANGIOLEIOMYOMATOSIS (LAM)

- Proliferation of **perivascular epithelioid cells** that express markers of both **melanocytes & SMCs**. The proliferation leads to **cystic, emphysema-like dilation of terminal airspaces**, **thickening of the interstitium**, **& obstruction of lymphatic vessels**
- Most often in **YOUNG WOMEN** of **CHILD-BEARING AGE**
- **ETIOLOGY:** loss of function mutation in tumor suppressor TSC2
- **CLINICAL:** dyspnea, spontaneous pneumothorax



INFLAMMATORY MYOFIBROBLASTIC TUMOR

- A tumor with a variable mixture of collagen, inflammatory cells, & myofibroblasts
- Common in **CHILDREN** of both genders
- **ETIOLOGY:** activating rearrangements of the anaplastic lymphoma kinase (ALK) gene
- **CLINICAL:** fever, cough, CP, & hemoptysis
- **TREATMENT:** surgery & ALK kinase inhibitors
- **PROGNOSIS:** excellent, but 5% have metastasis, invasion, & recurrence

LUNG NEOPLASMS

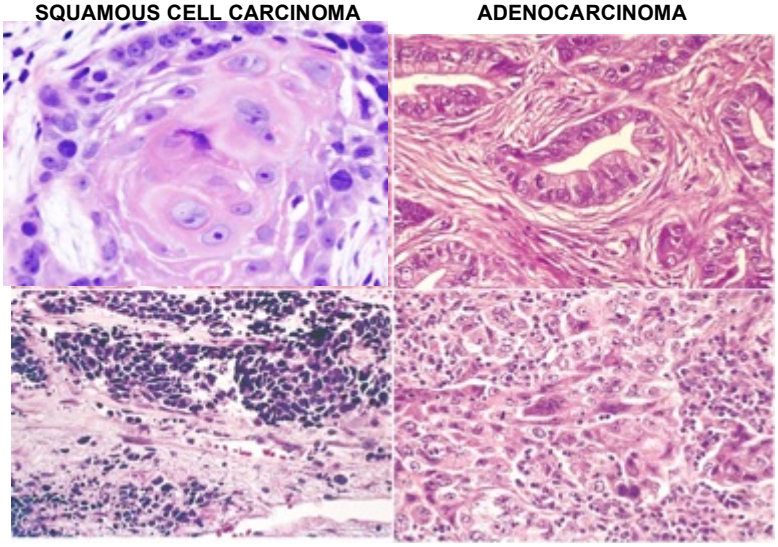
Bronchogenic Carcinomas*: Squamous Cell Carcinoma, Adenocarcinoma, Large Cell Carcinoma, Small Cell Carcinoma*

BRONCHOGENIC CARCINOMA

- 'Bronchogenic' refers to origin in the bronchial or bronchiolar epithelium
- Bronchogenic carcinomas encompass 4 major groups: squamous cell, adenocarcinoma, large cell, & small cell carcinoma – **Accounts for 90-95% of tumors of the lung**
  - **PERIPHERAL vs. CENTRAL LOCATION IS IMPORTANT IN DETERMINING TYPE****
- One of the most insidious & aggressive neoplasms
- **ETIOLOGY: CIGARETTE SMOKING** (90% of cases),** environmental pollutants, **radon gas (2nd most common cause of lung cancer in US)**
- **PATHOGENESIS:** oncogenes & the frequent loss/inactivation of tumor suppressor genes in most lung cancers
  - ONCOGENES
    - **c-MYC (nuclear TF) in small cell carcinomas**
    - Fragile Histidine Triad gene (**FHIT**) in **small cell carcinoma**
      - *FHIT gene is located on chromosome 3, which is commonly affected by translocations & deletion in human neoplasms*
    - **K-RAS in adenocarcinomas**
  - TUMOR SUPPRESSOR GENES
    - P53 & RB
- FREQUENT SITES FOR METASTATIC SPREAD: **ADRENALS (>50%),** liver (30-50%), brain (20%), bone (20%)

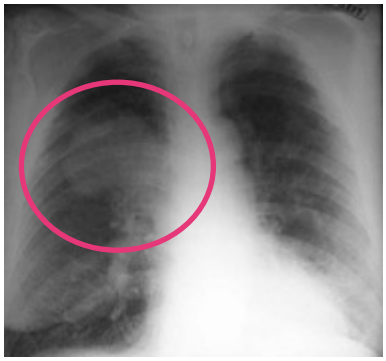
CLASSIFICATION OF LUNG TUMORS

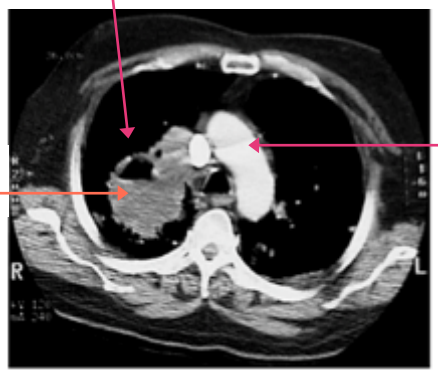
- **NON-SMALL CELL CARCINOMAS (NSCLC):** amenable to surgery & less so to chemotherapy/radiation
  - Squamous cell carcinoma (20%)
  - **Adenocarcinoma (38%)**
  - Large cell carcinoma (3%)
- **SMALL CELL LUNG CARCINOMAS (SCLC):** (14%) a systemic disease not amenable to surgery, but can be treated with chemotherapy & radiation

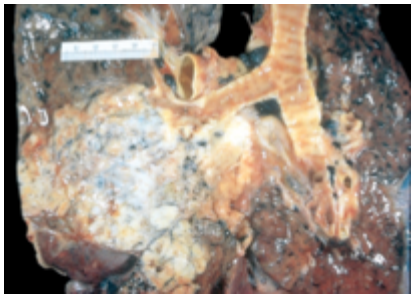


1. SQUAMOUS CELL CARCINOMA – NSCLC

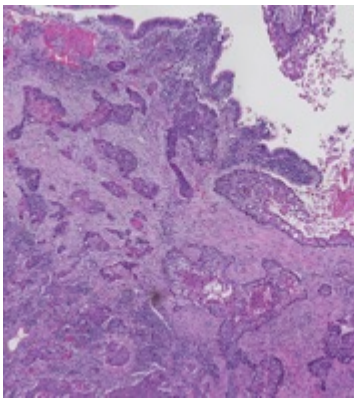
- *Slow growing malignant neoplasm composed of cells showing squamous differentiation* ***(metaplasia from smoke irritation)***
- Strong associated with **CIGARETTE SMOKING***
- More common in **OLDER MALES**
- **CLINICAL:** cough (75%), weight loss (40%), chest pain (40%), dyspnea (20%)
  - Hemoptysis
  - **Paraneoplastic syndromes – hypercalcemia (PTHrP)**
- **CENTRAL** large or small ill-defined mass
  - *"hilar lesion" or "associated with trachea"*
- **Immunostain with p53**
- Graded based on degree of differentiation
- Well differentiated – keratin pearl formation; intracellular bridges; cytoplasmic keratinization
- Endobronchial & invasive growth with **obstruction** into the lung parenchyma, peribronchial soft tissue, & adjacent lymph nodes
- Intraluminal & submucosal growth
- **Cavitation** – eccentric with thick wall
- **TREATMENT:** surgery + radiation

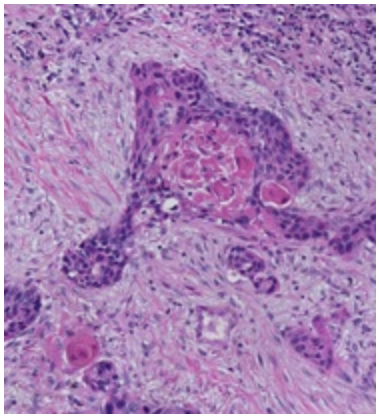






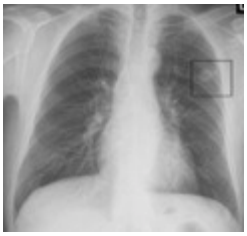
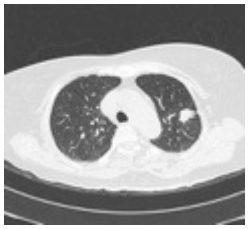
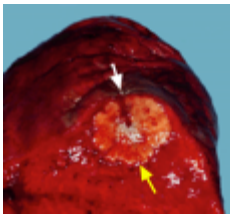
SQUAMOUS CELL CARCINOMA
Started central, then spread out

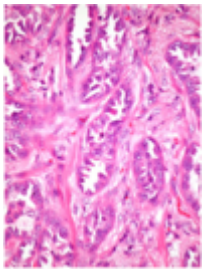




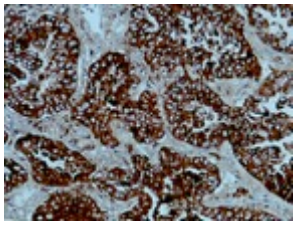
2. ADENOCARCINOMA – NSCLC – Most common NSCLC (28%)

- *Malignant neoplasms of glandular epithelial cells forming glands & papillary elements often with mucin production*
- AKA "Scar Carcinoma" – *May originate in a scar*
- Most common in **OLDER FEMALES & NON-SMOKERS**
- **PRECURSOR: atypical adenomatous hyperplasia**
- Small or large ill-defined mass, more **PERIPHERALLY** (parenchyma or pleural) location
- Cavitations are rare
- **Immunostain: TTF-1 or Napsin**
- **PATHOLOGY:** Forming glands & producing mucin
  - **Central necrosis in malignant neoplasms**
- **TREATMENT:** surgery or radiation, Bevacizumab (Avastin) monoclonal antibody to VEGF used for adenocarcinoma, but NOT squamous cell

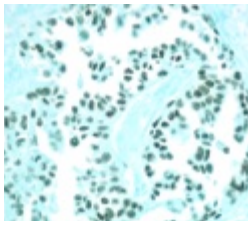




TTF1

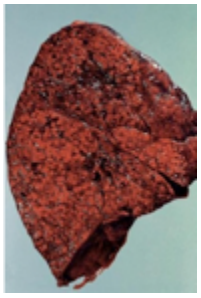
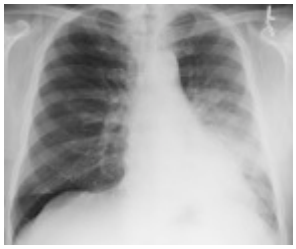


Napsin

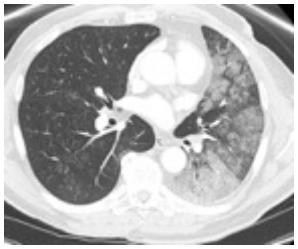


BRONCHIOLOALVEOLAR CARCINOMA – Adenocarcinoma in situ

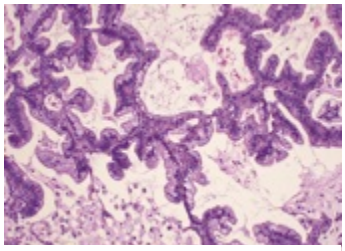
- Subtype of adenocarcinoma characterized by the growth of malignant glandular cells along the alveolar framework (lepidic spread) without invasion
- Localized or diffuse & may be bilateral
- Tall columnar to low cuboidal mucus producing cells that line along alveolar septae without destruction of the alveolar pattern of the lung
- **PATHOGENESIS:** arise in the terminal bronchoalveolar region from Clara cells (non-ciliated peg-like cell in the terminal bronchiole) or type II pneumocytes
- **PATHOLOGY:** spread aerogenously
  - Mucinous tend to spread (solitary or multiple nodules)
  - Non-mucinous rarely spread (solitary nodule)

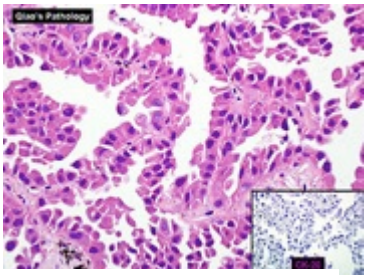
CXR: Hazy infiltrate



CT: Alveolar filling (air bronchogram)



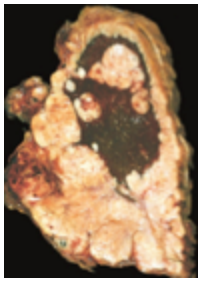
MUCINOUS



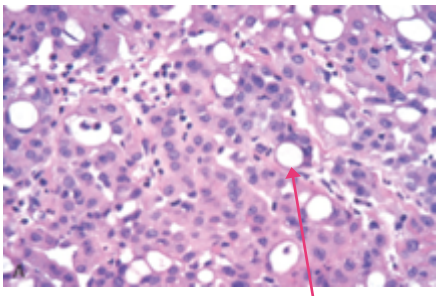
NON-MUCINOUS

MALIGNANT MESOTHELIOMA *(From Pathoma - Marked as HY there)*

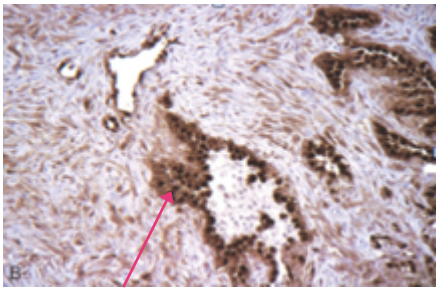
- *Rare highly malignant cancer that arises from the mesothelial cells of pleural & peritoneum*
- Most often in **OLDER MALE** w/ **pain**, dyspnea, & **RECURRENT PLEURAL EFFUSIONS**
- **ASBESTOS exposure** gives an increased incidence
  - *Presents first with **pleural diaphragmatic plaques!***
- 50% of patients die within 12 months of diagnosis; few survive longer than 2 years
- **HISTOLOGY:** epithelioid cells (**ROUND CELLS**; glandular formation) or sarcomatoid cells (**SPINDLE CELLS***)
- **IMMUNOSTAINS**: keratin, calretinin, Wilms Tumor 1 (WT-1), cytokeratin 5/6, & D2-40



Thick, firm white PLEURAL TUMOR encasing the lung



Glands forming – therefore EPITHELIOID (ROUND CELLS)



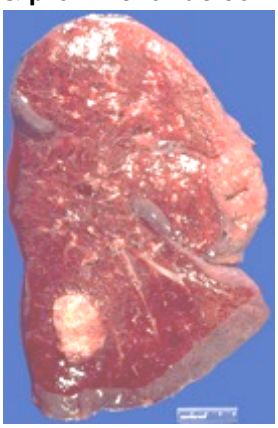
Sarcomatoid cells - elongated SPINDLE-SHAPED
Glandular formation – epithelioid cells - ROUND

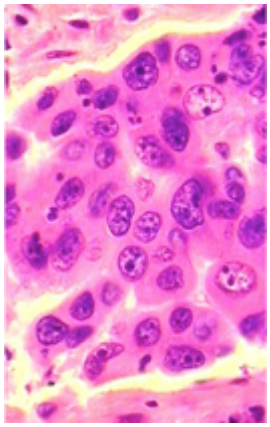
DIFFERENTIATE BETWEEN MESOTHELIOMA & ADENOCARCINOMA

- MESOTHELIOMA stains **POSITIVE for KERATIN & CALRETININ & NEGATIVE for CEA**
  - *CEA: tumor marker (Ag secreted by the tumor; typically used in colon cancer)*
- MICROVILLI ON EM
  - MESOTHELIOMA – LONG, SLENDER MICROVILLI
  - ADENOCARCINOMA – SHORT & BLUNTED MICROVILLI

3. LARGE CELL CARCINOMA - NSCLC

- Tumor cells are large & anaplastic
  - Cells are atypical, bizarre, poorly-differentiated *without glandular or squamous differentiation*
- Very rapid growth
- Cavitation infrequent
- Early hematogenous & lymphatic spread
- **PATHOLOGY**
  - Dx of exclusion – no squamous or glandular markers
  - **GROSS** – bulkly, soft gray, tan, or pink masses with **extensive necrosis**
  - 50% arise in subsegmental or larger bronchi
  - 50% of peripheral & subpleural in location
  - **A GIANT CELL type exists characterized by numerous large cells, each containing several bizarre, pleomorphic nuclei & prominent nucleoli**

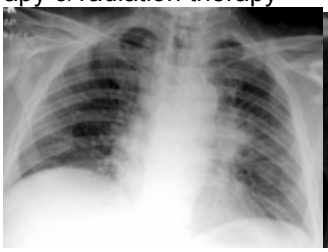


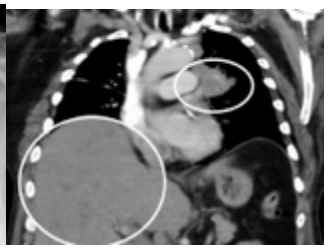


4. SMALL CELL CARCINOMA - SCLC

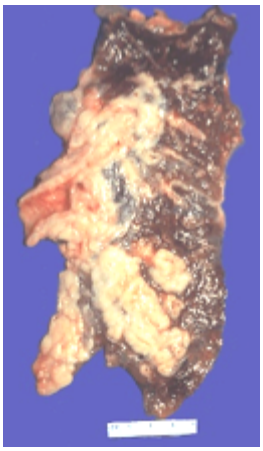
- Most AGGRESSIVE carcinoma – SURGERY IS NOT AN OPTION!
- AKA Oat Cell Carcinoma; Small cell anaplastic carcinoma; Undifferenciated small cell carcinoma
- Associated with **CIGARETTE SMOKING** & radiation exposure**
- Tumor cells resemble lymphocytes (small, very little cytoplasm)
- Early hematogenous spread
  - **Staging (spreading potential) more important** than grading (differentiation status)!
- Highest correlation with the paraneoplastic syndrome
- EM: dense core **neurosecretory grauules**
- May be **CENTRAL/HILAR** or PERIPHERAL
  - *Smoking + central mass → look at biopsy to differentiate between small cell & squamous cell*
  - *Smoking + peripheral mass → small cell most likely*
  - *Non-smoking + peripheral mass → adenocarcinoma most likely*
- **TREATMENT**: chemotherapy & radiation therapy

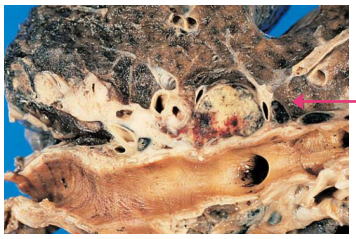
Left hilar mass
Linear Atelectasis LLL



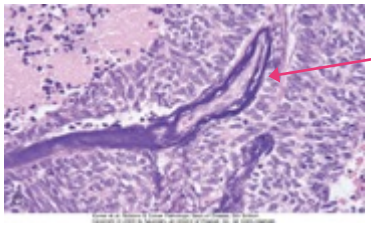


Left hilar mass
Metastatic liver disease

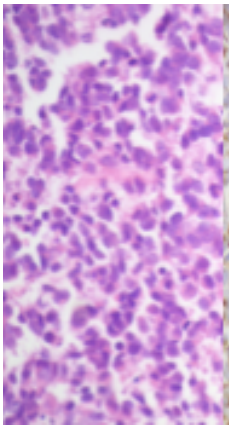




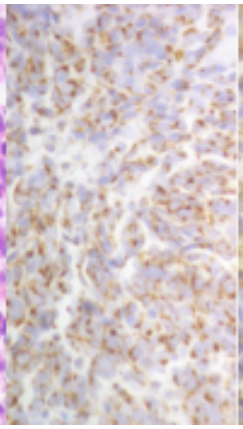
Small cell carcinoma growing along the bronchus



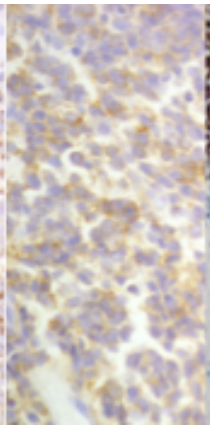
AZZOPARDI EFFECT – condensation of chromatic around the blood vessel



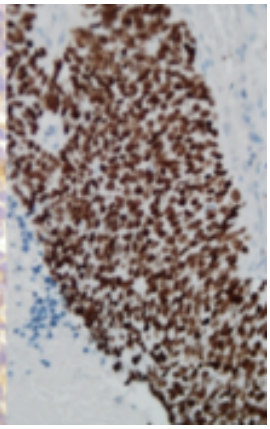
H&E stain



Keratin-dot in cytoplasm

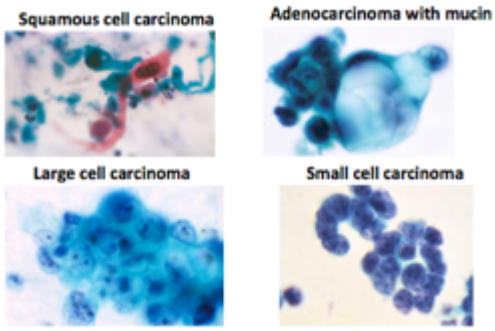


Chromogranin in cytoplasm



TTF-1 nuclear

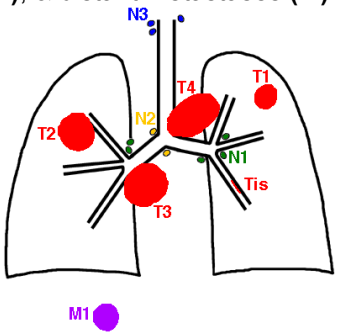
CYTOLOGIC DIAGNOSIS OF LUNG CANCER



STAGING OF LUNG CANCER

- Stage = spread
- Grade = differentiation
- Lung cancers are staged according to the **TNM** staging system, which takes into account the tumor size & location **(T)**, lymph node metastases **(N)**, & distant metastases **(M)**

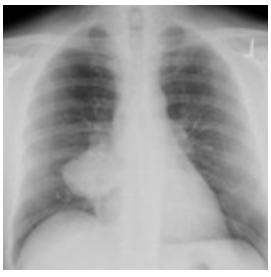
STAGE GROUPING for NON-SMALL CELL CARCINOMA

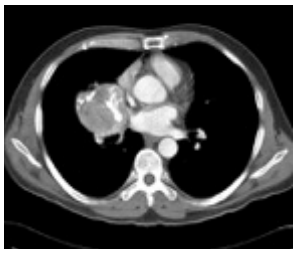


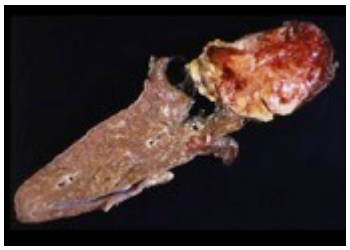
- Staging Small Cell Carcinoma
  - Limited-stage disease: tumor confined to the hemithorax of origin, the mediastinum, & the supraclavicular nodes, which can be encompassed within a tolerable radiation therapy port.
  - Extensive-stage disease

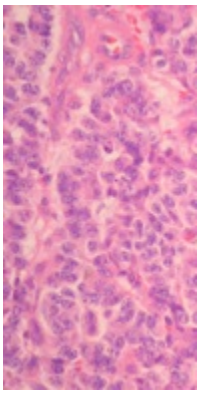
CARCINOID TUMOR

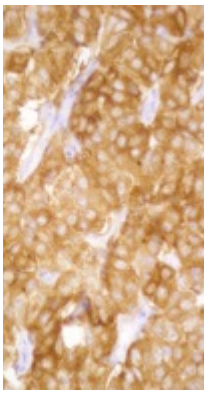
- *Carcinoid – derived from neural crest cells*
- 1-5% of all tumors
- Most patients **UNDER AGE OF 40**
- Causes symptoms by intraluminal growth
  - Mass in the lumen – causes obstructive problems → *Atelectasis, pneumonia, bronchiectasis*
- Resemble intestinal carcinoids & may rarely be associated with the carcinoid syndrome (flushing of the face)
- **PATHOLOGY:** salt & pepper nuclei
- **Dense core granules** on EM
- **POSITIVE FOR KERATIN & NE MARKERS**
- **TREATMENT**: SURGERY
- Associated with Multiple Endocrine Neoplasia (MEN1)







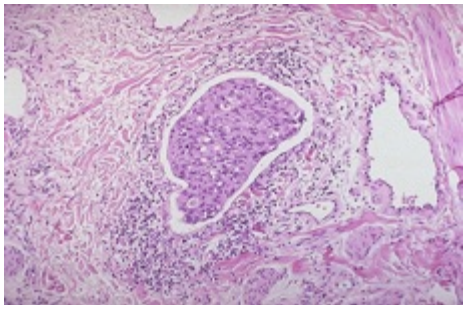




Synaptophysin

LUNG & METASTATIC DISEASE

- Lung tumors metastasize to: regional nodes, adrenals, liver, brain, & bone
- The lungs receives hematogenous & lymphatic metastases from: breast, GI, sarcomas, melanoma, etc.
- Mucinous lung primaries also spread aerogenously within lung



A nest of metastatic infiltrating ductal carcinoma from the breast is seen in a dilated lymphatic channel in the lung. Carcinoma can have a "lymphangitic“ pattern in which streaks of tumor appear between lung lobules and beneath the pleura in lymphatic spaces.