Interstitial Lung Disease

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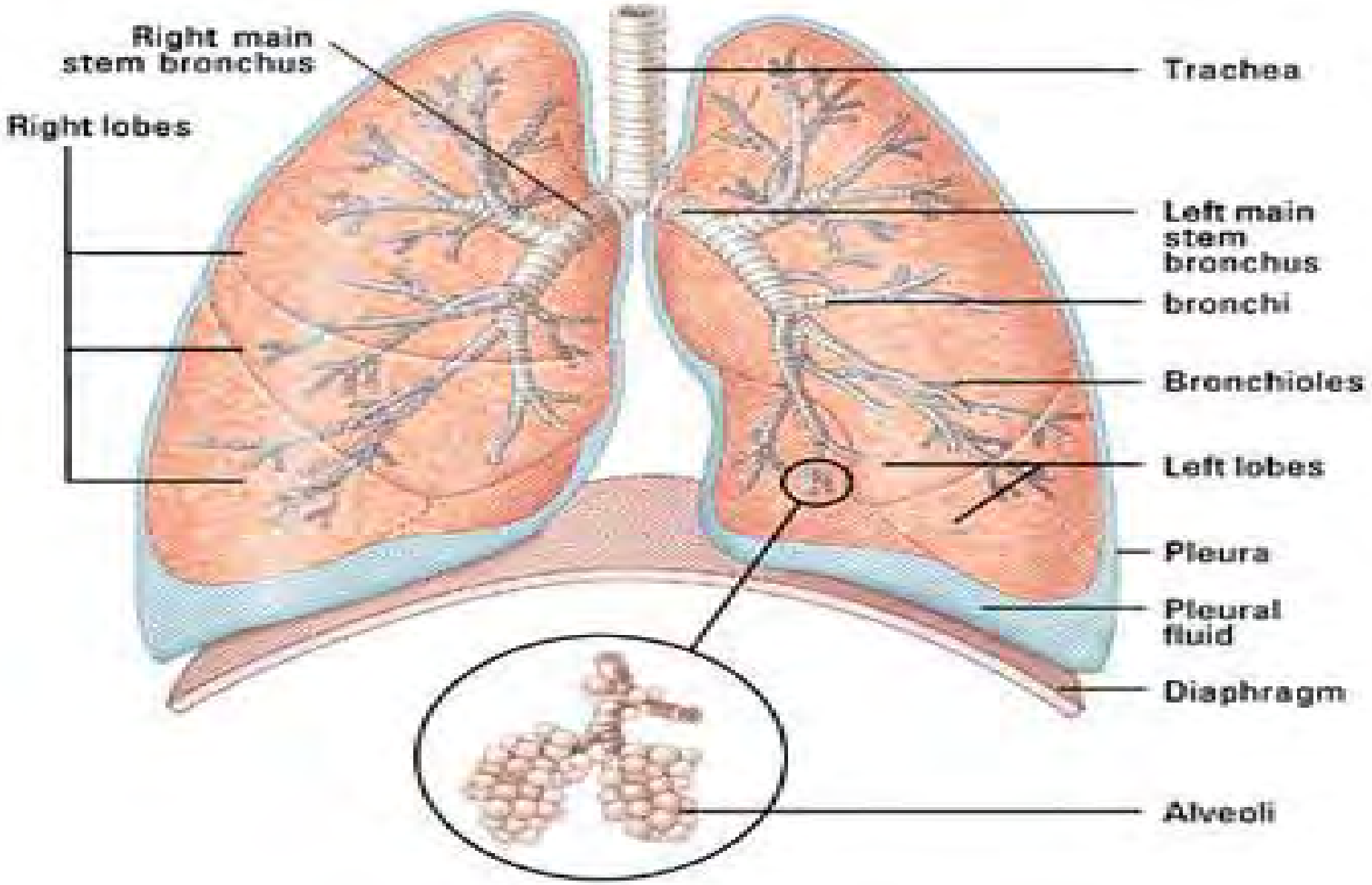
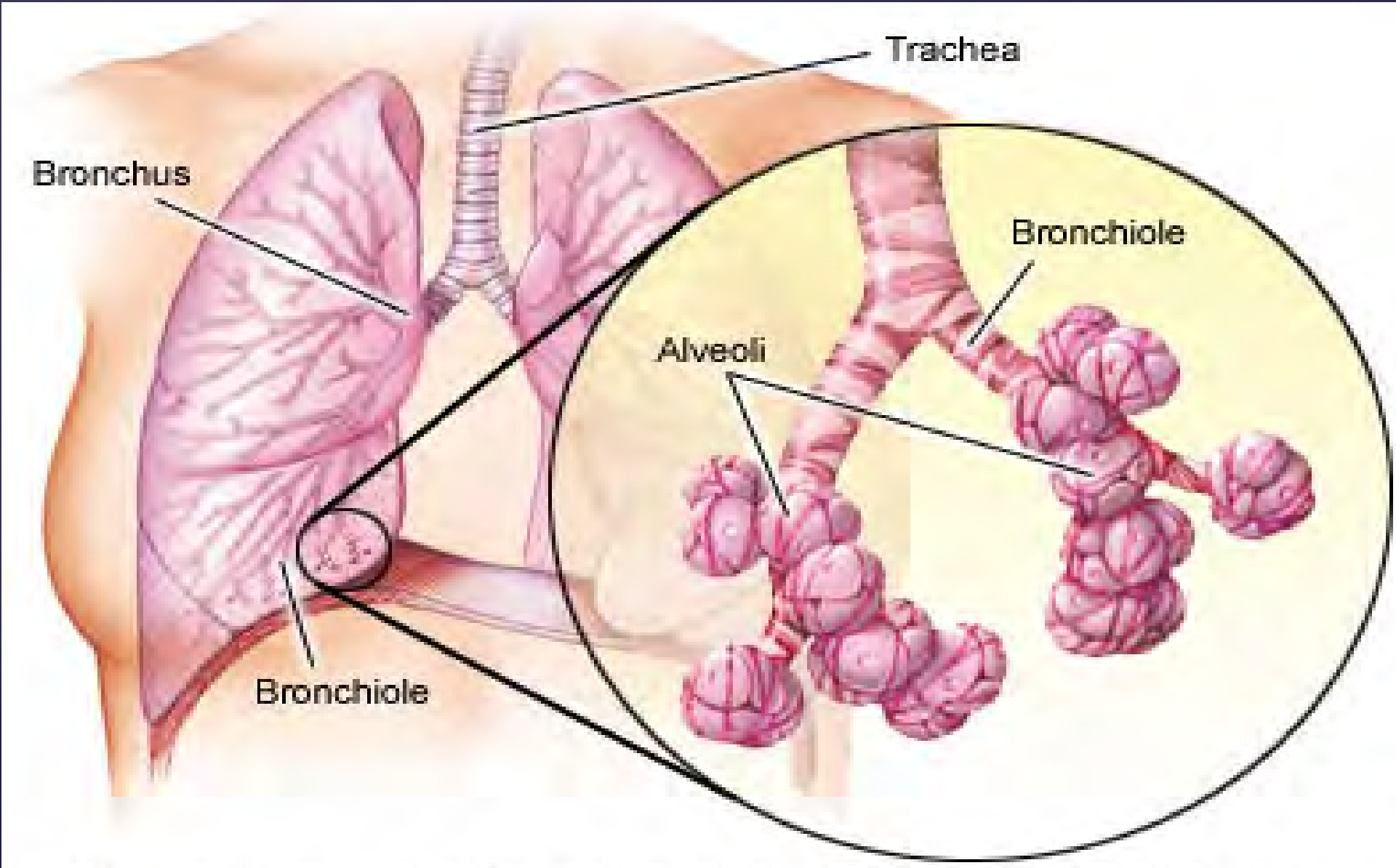
Lungs


Right main stem bronchus
Right lobes
Trachea
Left main stem bronchus
bronchi
Bronchioles
Left lobes
Pleura
Pleural fluid
Diaphragm
Alveoli

Lung Physiology



ILD Classification

Connective Tissue Diseases
Scleroderma
Polymyositis-Dermatomyositis
Systemic Lupus Erythematosus
Rheumatoid Arthritis
Mixed Connective Tissue Disease
Ankylosing Spondyitis

Primary (Unclassified)
Sarcoidosis
Langerhans cell histiocytosis
Amyloidosis
Pulmonary vasculitis
Lipoid pneumonia
Lymphangitic carcinomatosis
Bronchoalveolar carcinoma
Pulmonary lymphoma
Gaucher's Disease
Niemann-Pick Disease
Hermansky-Pudlak syndrome
Neurofibromatosis
Lymphangioleiomyomatosis
Tuberous Sclerosis
ARDS
AIDS
Bone Marrow Transplantation
Postinfectious
Eosinophilic pneumonia
Alveolar Proteinosis
Diffuse Alveolar Hemorrhage Syndromes
Alveolar microlithiasis
Metastatic calcification

Treatment-Related / Drug-Induced
Antibiotics – nitrofurantoin, sulfasalazine
Antiarrhythmics – amiodarone, propanolol
Anti-inflammatories – gold, penacillamine
Anti-convulsants – dilantin
Chemotherapeutic agents – bleomycin, cyclophosphamide, methotrexate, azathioprine
Therapeutic radiation
Oxygen toxicity
Narcotics

Occupational and Environmental Diseases

Inorganic

Silicosis
Asbestosis
Hard-metal pneumoconiosis
Coal worker's pneumoconiosis
Berylliosis
Aluminum oxide fibrosis
Talc pneumoconiosis
Siderosis (arc welder)
Stannosis (tin)

Organic

Bird breeder's lung
Farmer's lung
Bacteria – e.g. NTB mycobacteria
Fungi – e.g. Aspergillus
Animal protein – e.g. Avian
Chemical sensitizers - e.g. isocyanates

Idiopathic Fibrotic Disorders
Acute interstitial pneumonitis (Hamman-Rich syndrome)
Idiopathic Pulmonary Fibrosis
Familial Idiopathic Pulmonary Fibrosis
Desquamative intersitial pneumonitis
Respiratory bronchiolitis
Cryptogenic organizing pneumonia
Nonspecific interstitial pneumonitis
Lymphocytic interstitial pneumonia (Sjögrens Syndrome, AIDS, Hashimoto's)
Autoimmune pulmonary fibrosis (inflammatory bowel disease, PBC, ITP, AIHA)

Interstitial Lung Disease

Connective Tissue Diseases

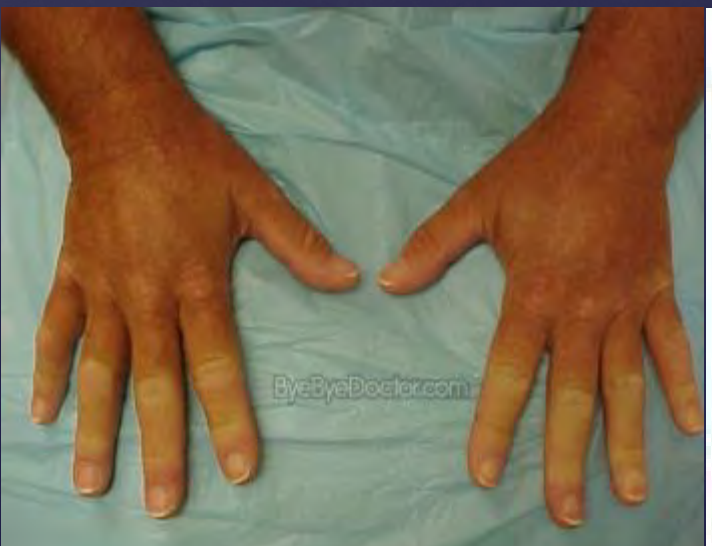
Primary (unclassified)

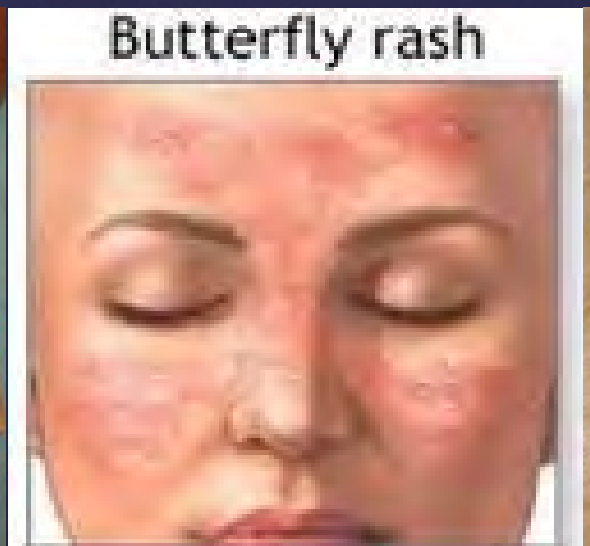
Idiopathic Fibrotic Disorders

Drug and Treatment Induced

Connective Tissue Diseases

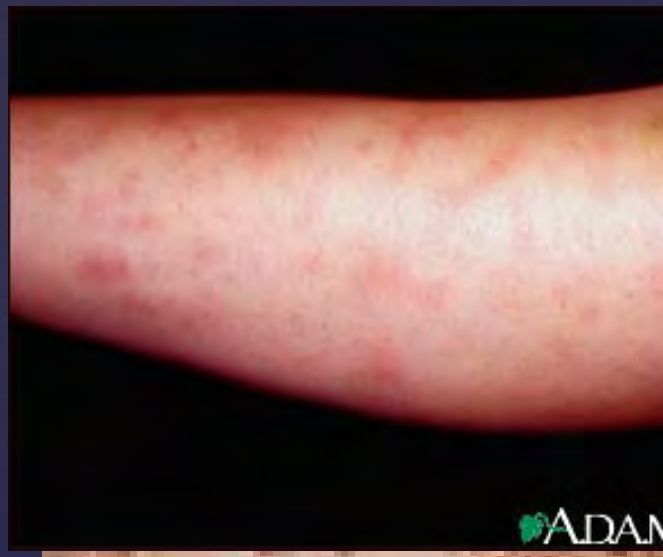
- Scleroderma
- Systemic Lupus Erythematous (SLE)
- Rheumatoid Arthritis
- Mixed Connective Tissue Disease

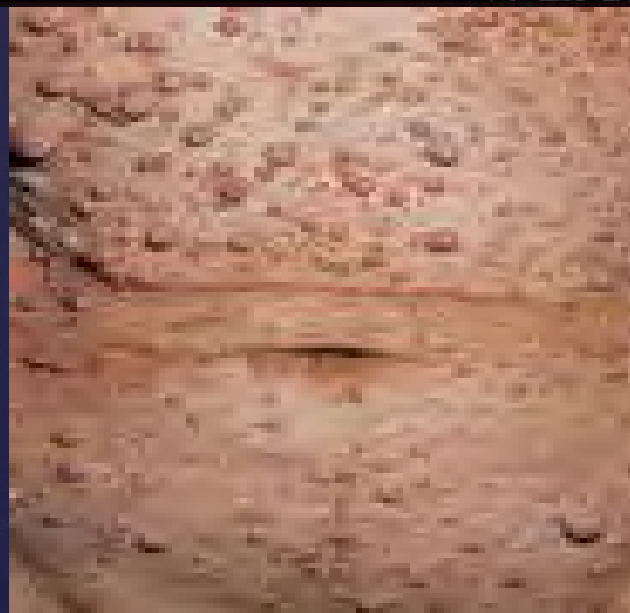




Primary (unclassified)

Sarcoidosis Stage I-IV
Neurofibromatosis
Tuberous Sclerosis
AIDS
ARDS
Bone Marrow Transplantation
Post infectious





Occupational & Environmental Exposures: Inorganic & Organic

Agriculture Workers and Animal Handlers

Construction: wood/metal

Auto repair

Military

Chemicals (plastic, paint, polyurethane)

Organisms: fungus/molds/bacterium

Idiopathic Fibrotic Disorders

Pulmonary fibrosis

Familial pulmonary fibrosis

Autoimmune pulmonary fibrosis

Respiratory bronchiolitis

Nonspecific interstitial pneumonitis (NSIP)

Drug Induced

Antibiotics

Anti-arrhythmics

Anti-inflammatory

Anti-convulsant

Radiation/Chemotherapy

Oxygen toxicity

Narcotics

ILD Epidemiology in the US

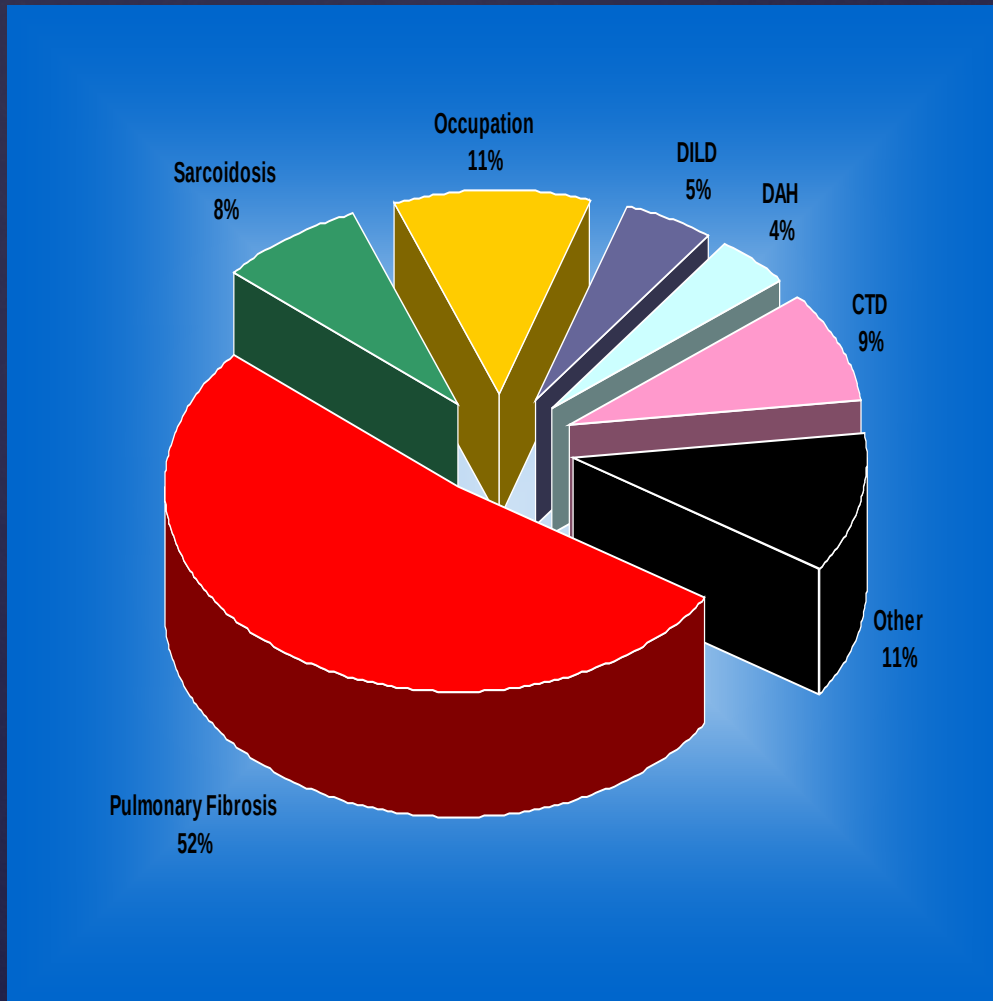
100K admissions/year

15% pulmonologist patients

Incidence: 5/100K

Men (31%) versus Women (26%)

IPF 45% of all ILD patients



Age/Gender/Race Specifications to Assist in Diagnosis

20-40yrs:

Inherited Interstitial Lung diseases
Familial idiopathic pulmonary fibrosis
Collagen vascular disease- associated ILD
LAM
Pulmonary Langerhans' cell granulomatosis
Sarcoidosis

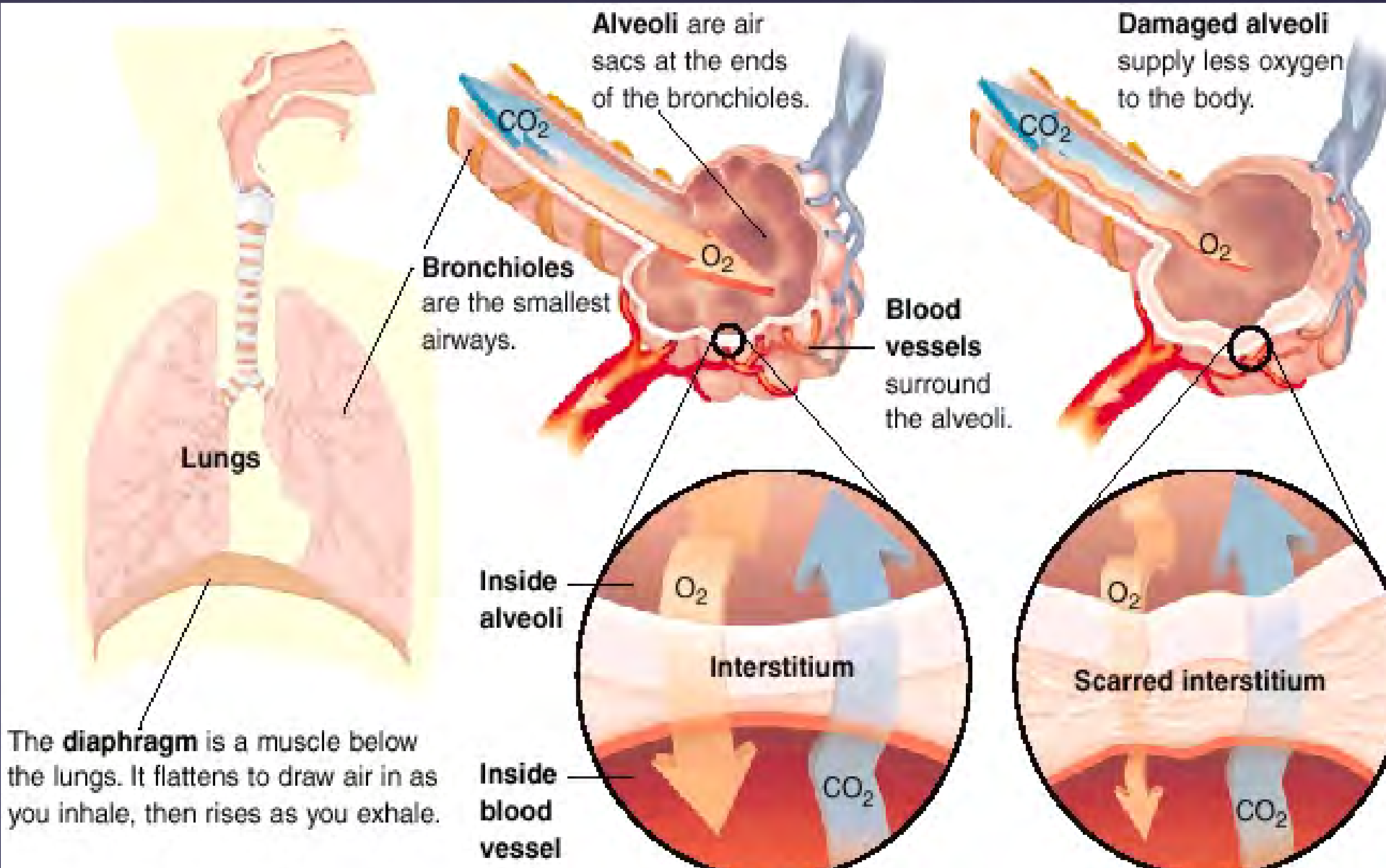
50yrs:

IPF

Females: CVD, LAM, Tuberous Sclerosis
Males: ILD with RA and pneumoconosis

AA 10-12x more often seen with Sarcoidosis

Pathophysiology of ILD



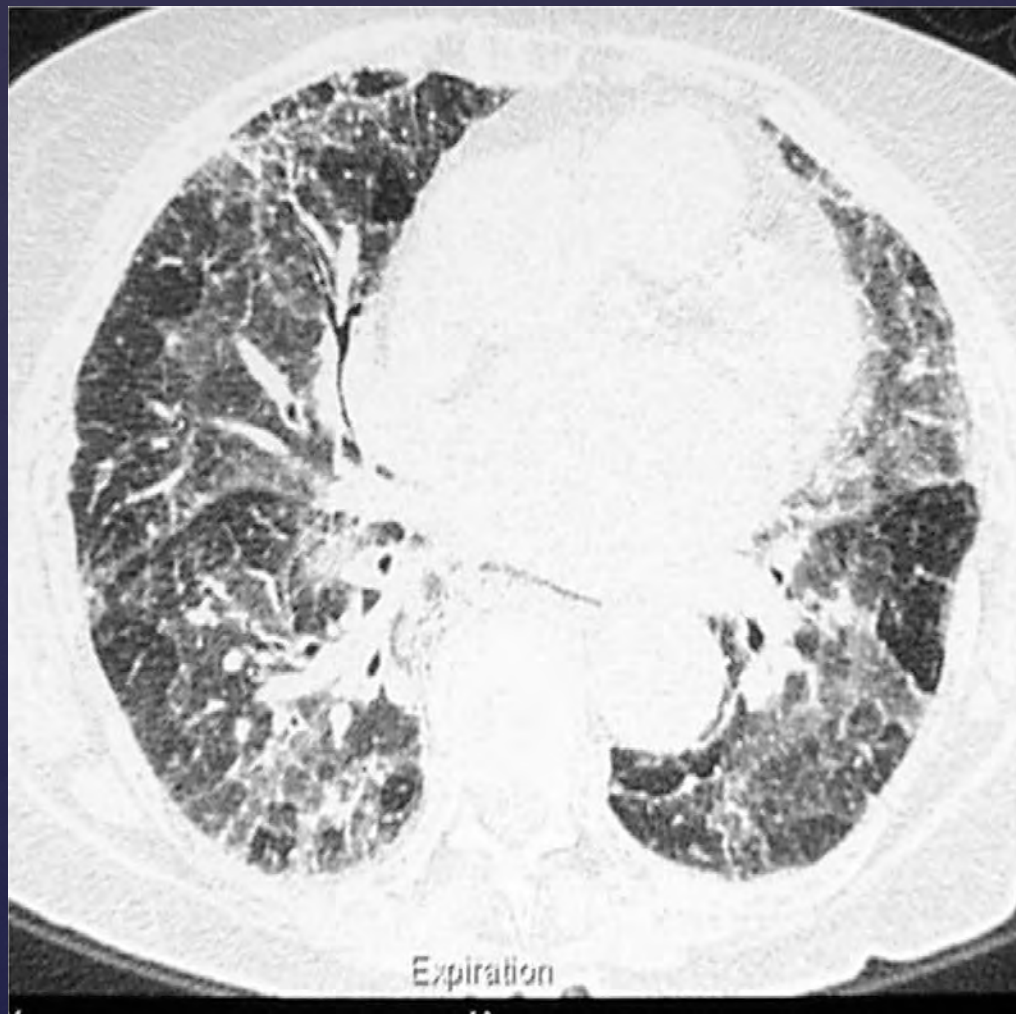
Pattern of Lung Injury/Repair/Scarring Histology

Cellular: Appears more inflammatory tends to be more responsive to treatment

Fibrotic: Appear more scarred which is **not** responsive to medicines and often requires lung transplantation

Heterogenous Group of Diffuse Parenchymal Lung Diseases

- Physiologic alterations
- Clinical symptoms
- Radiologic abnormalities
- Pathologic manifestations



Physiologic Alterations

Alveolar epithelial cells and basement membrane injury

Increased alveolar permeability

Spillage into alveolar space

Recruitment of fibroblasts

Stimulation of an inflammatory response

Unable to repair; scar forms; structural changes

Physiologic Abnormalities: Restrictive Lung Disease

Injury:

- Alveolar epithelial cells in the interstitium; changes lung architecture: alveolar walls, septa, peri-bronchial and perivascular spaces

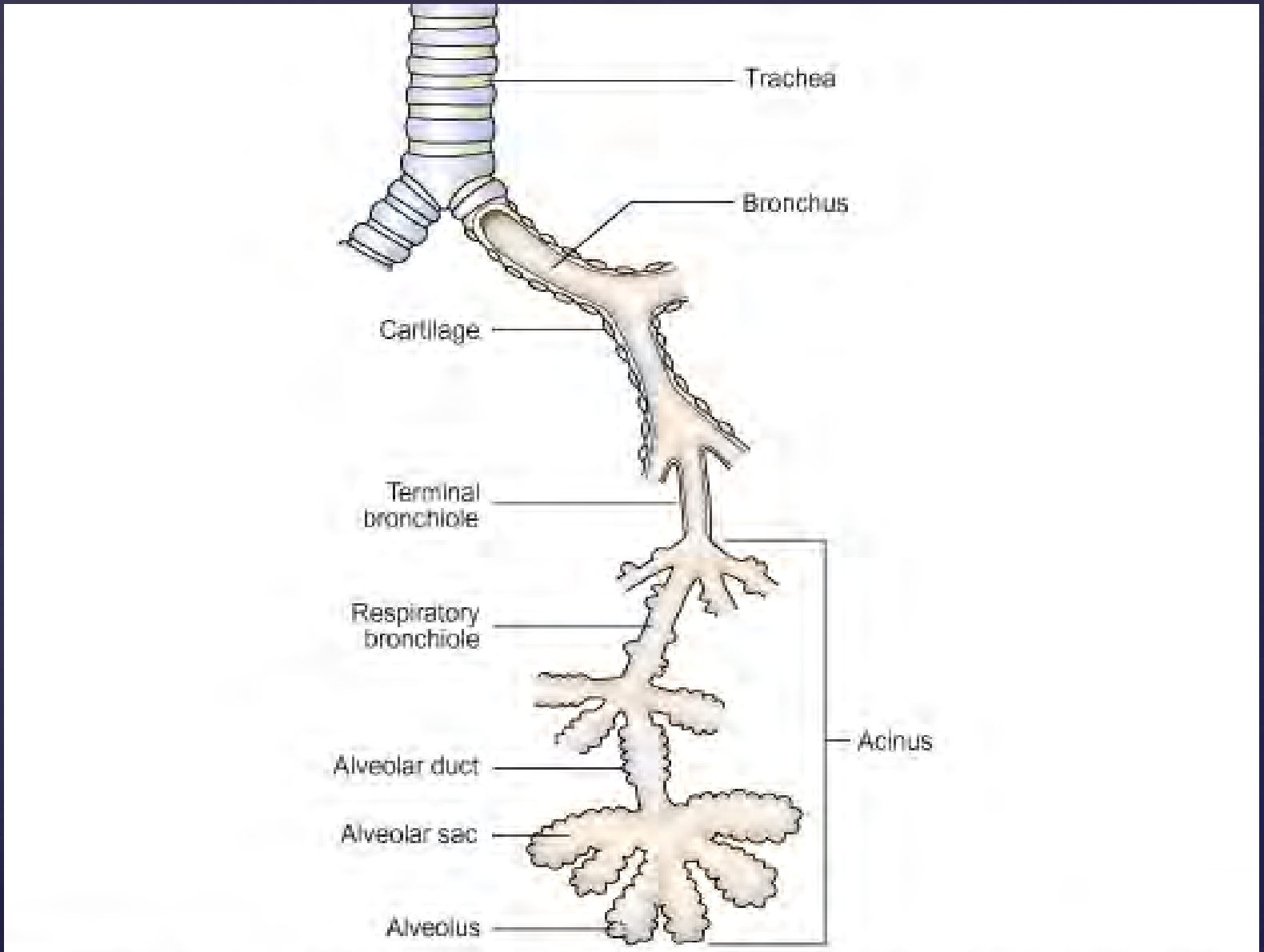
Inflammation:

- Distal lung parenchyma: alveolar wall/septa impacting loose-binding connective tissue to include: peri-bronchovascular sheaths, interlobular septa and visceral pleural

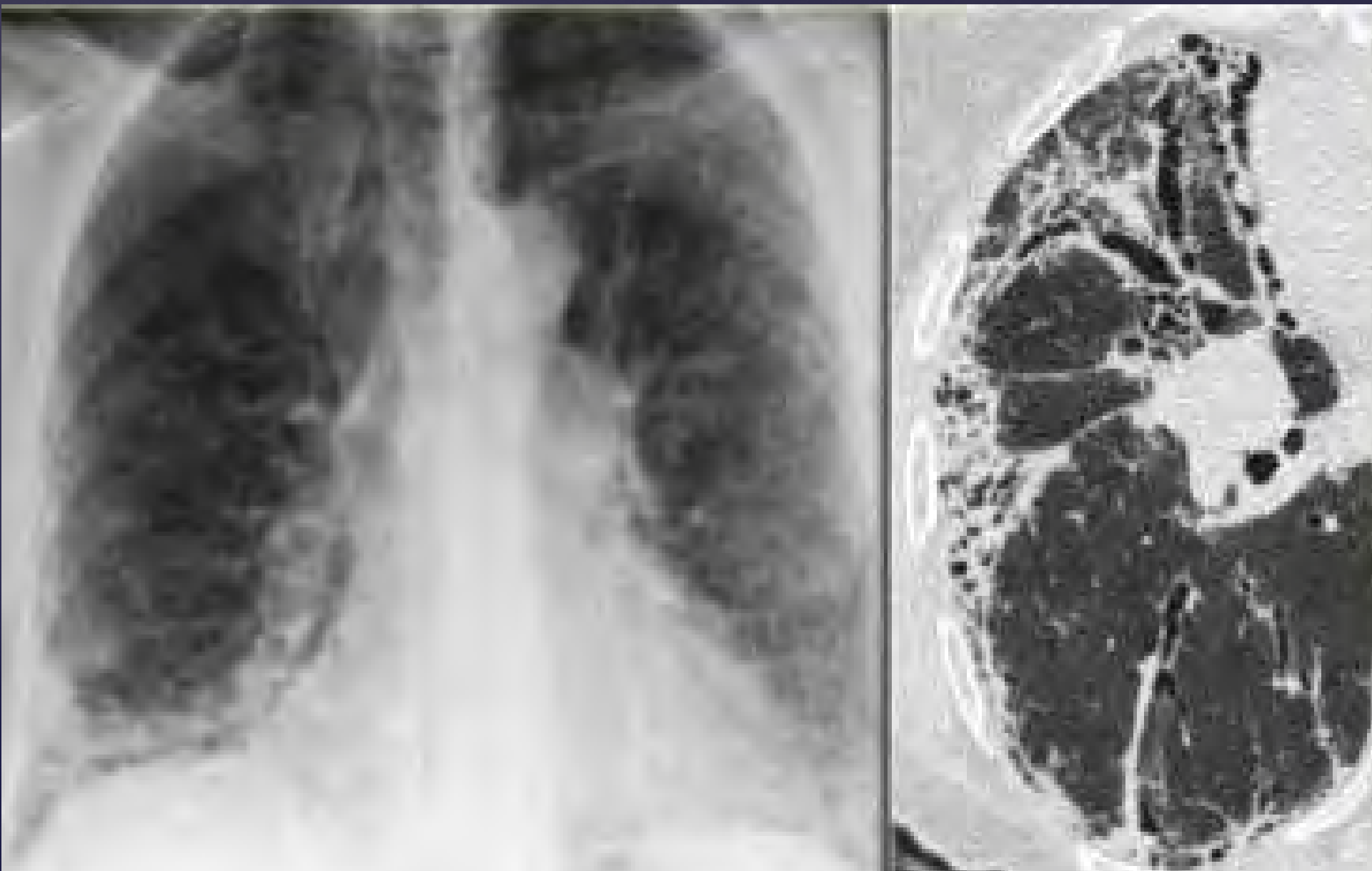
Scar formation:

- Permanent structural changes, impacting physiologic changes and symptoms

Injury … Inflammation …Scar…



Injury … Inflammation… Scar



Initial Work Up or Referral

History and Physical Exam

Chest Radiograph: CXR/CT

Pulmonary Function Testing

Other Diagnostics: EKG/Echo

Medication evaluation

Serologic Studies and Pathology

History

Symptoms:

- Worsening exertional dyspnea over past 6mos 2yrs
- Dry non-productive cough: r/o GERD/sinus disease/allergies
- Increased fatigue
- Decreased ability to perform ADLs
- Not appearing acutely ill

Past Medical/Family History:

- CTD, Cancer, Inflammatory Bowel, AR, Asthma, GERD, Dysphagia/Aspiration; Arthritis, Sinus Dz, Hemoptysis
- Family h/o: CTD: RA, SLE, Scleroderma

History

Exposures: Occupation/Environmental

Meds

Frequent Hospitalizations

Abnormal CXR/CT

Pathology report(s) if available

Acute Onset of Symptoms

Time: Days to Weeks

Symptoms: Rapid SOB

Diagnostics: Diffuse opacities, fevers

ILD Diseases:

- AIP (acute interstitial pneumonitis)
- Acute pneumonitis from CVD (especially SLE)
- COP (cryptogenic organizing pneumonia)
- Drugs
- DAH
- Eosinophilic lung disease
- Hypersensitivity pneumonitis

Sub-Acute Onset of Symptoms

Time: Weeks to months

Symptoms: Increased WOB

ILD Diseases/Causes

- Collagen vascular disease
- COP
- Sub-acute hypersensitivity pneumonitis
- Drugs

Chronic Symptoms

Time: Months to years

Symptoms: Mild progressive DOE; afebrile

Diagnostics: Bronchiectasis on CXR/CT

ILD Diseases/Causes:

- Chronic hypersensitivity pneumonitis
- Collagen vascular disease
- IPF and NSIP
- Occupation – related lung diseases

Typical ILD Physical Examination

Signs & Symptoms:

- Chronic, non-productive cough
- DOE
- Elevated HR/RR

Findings:

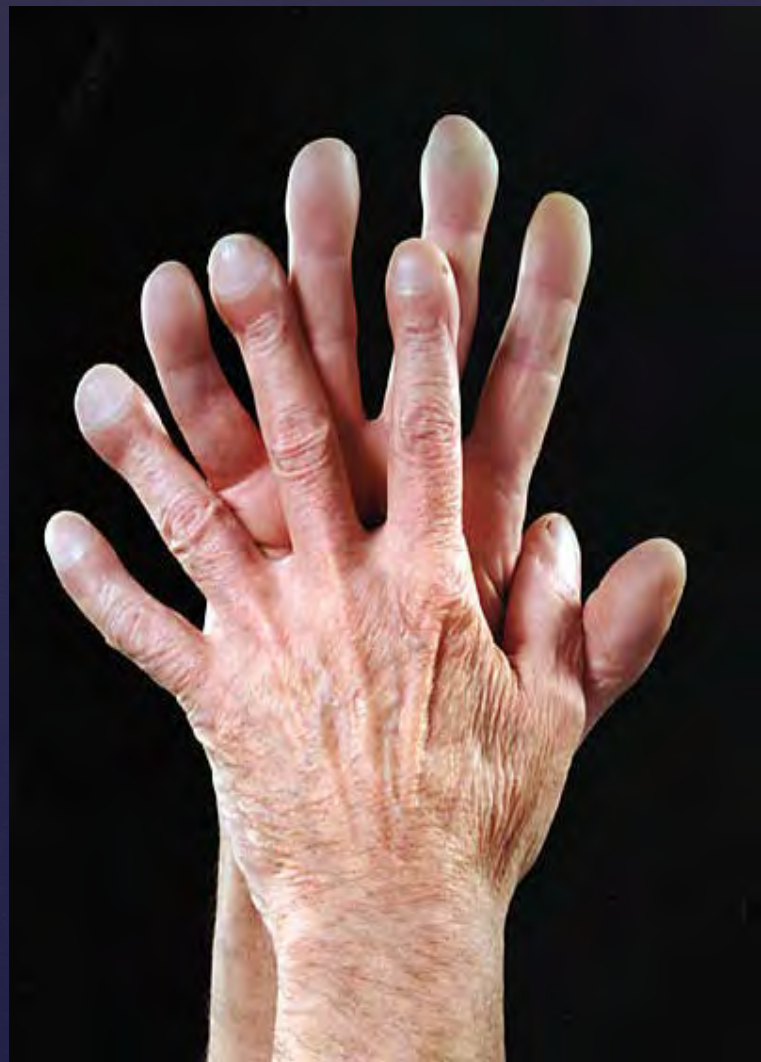
- Velcro rales/inspiratory bi-basilar crackles
- LE edema ® side
- Rash/discolored/scarred tissue
- Cyanosis/clubbing

Clubbing: Pathologic changes seen on Physical Exam

Distal digital vasodilation r/t hypoxia

Increased interstitial edema

Changes in vascular connective Tissue



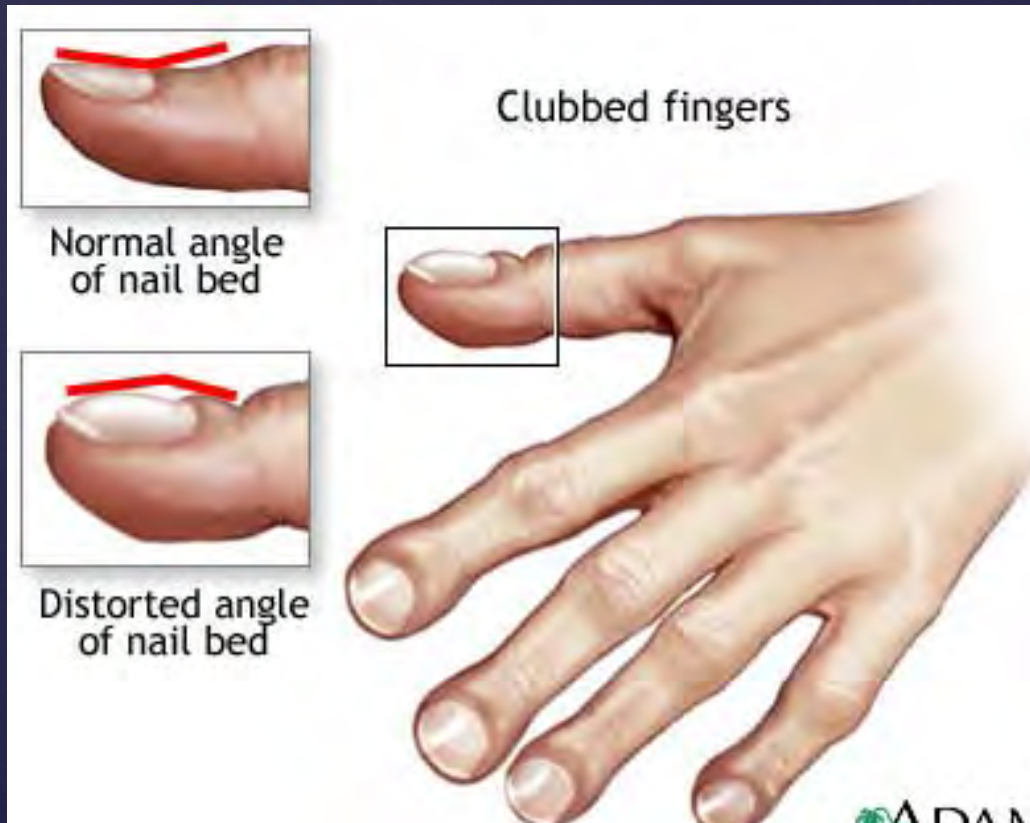
Impact on ILD

80% Respiratory disorder

25-50% IPF patients

50% DIP patients

75% ILD with R/A



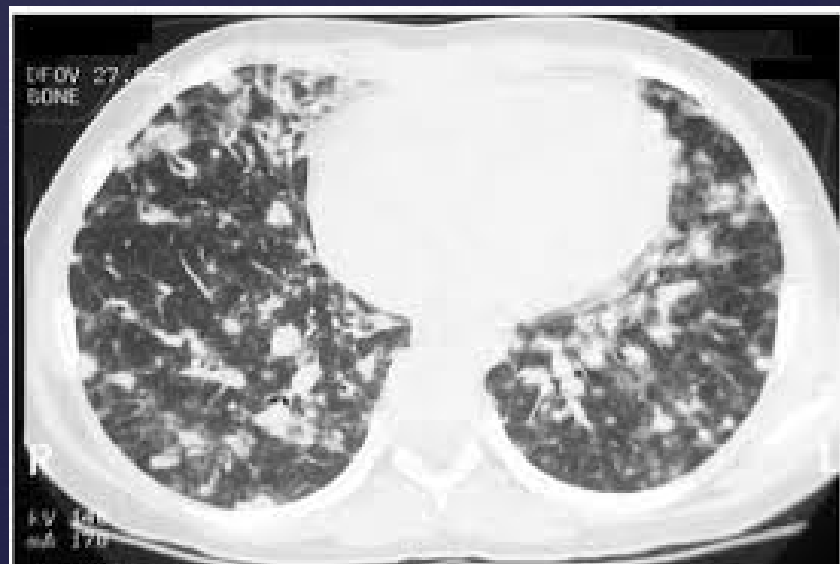
Common Radiologic Abnormalities: CXR or Chest CT in ILD

Interstitial Prominent Lung Markings

Fibrosis Traction Bronchiectasis

Ground glass opacities

Mosaic attenuation



ILD on CXR – Can be complex

10 to 15 % Symptomatic patients with proven infiltrative lung disease

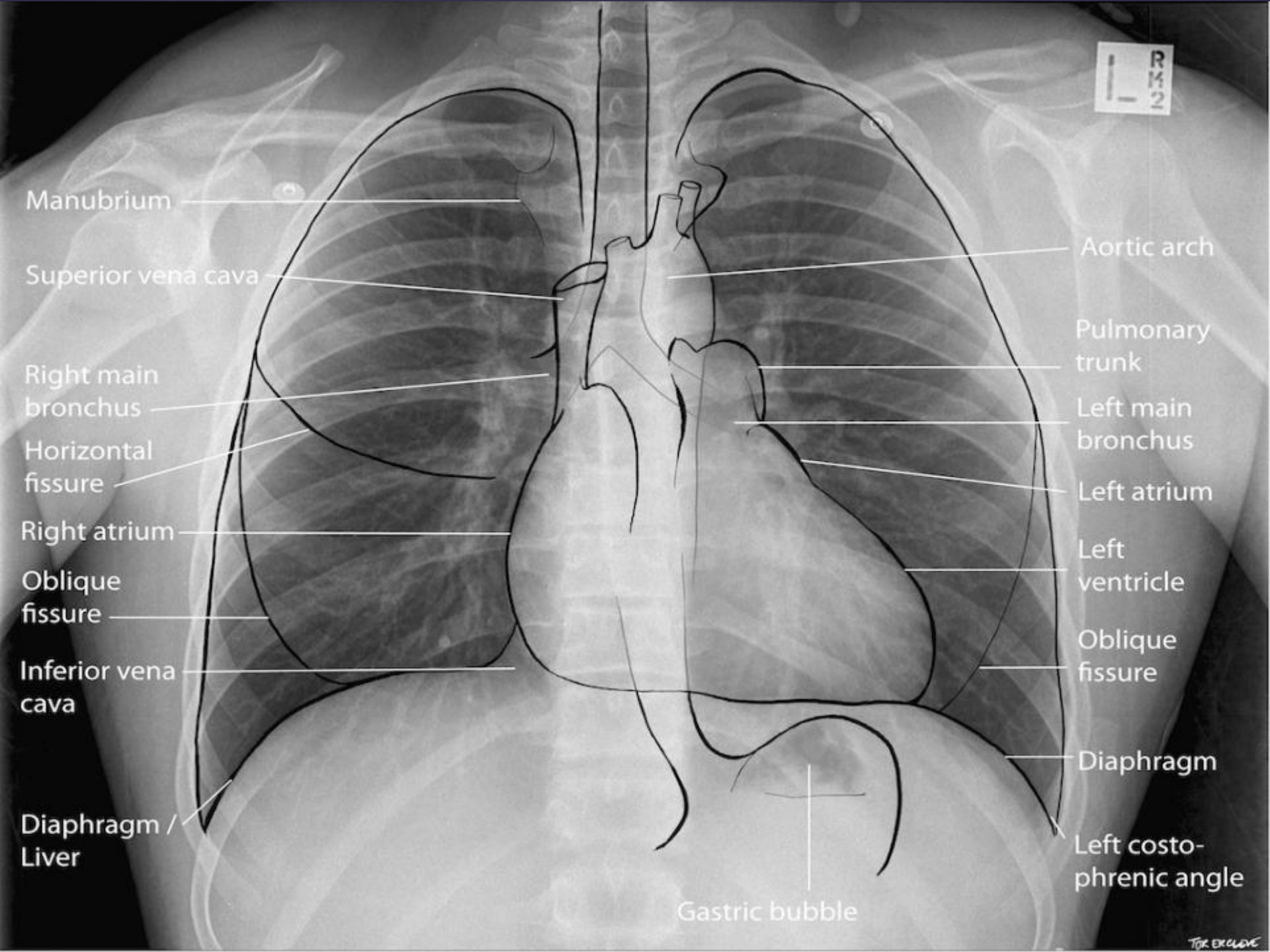
30% Bronchiectasis

60 % Emphysema patients

Sensitivity of 80% and Specificity of 82%

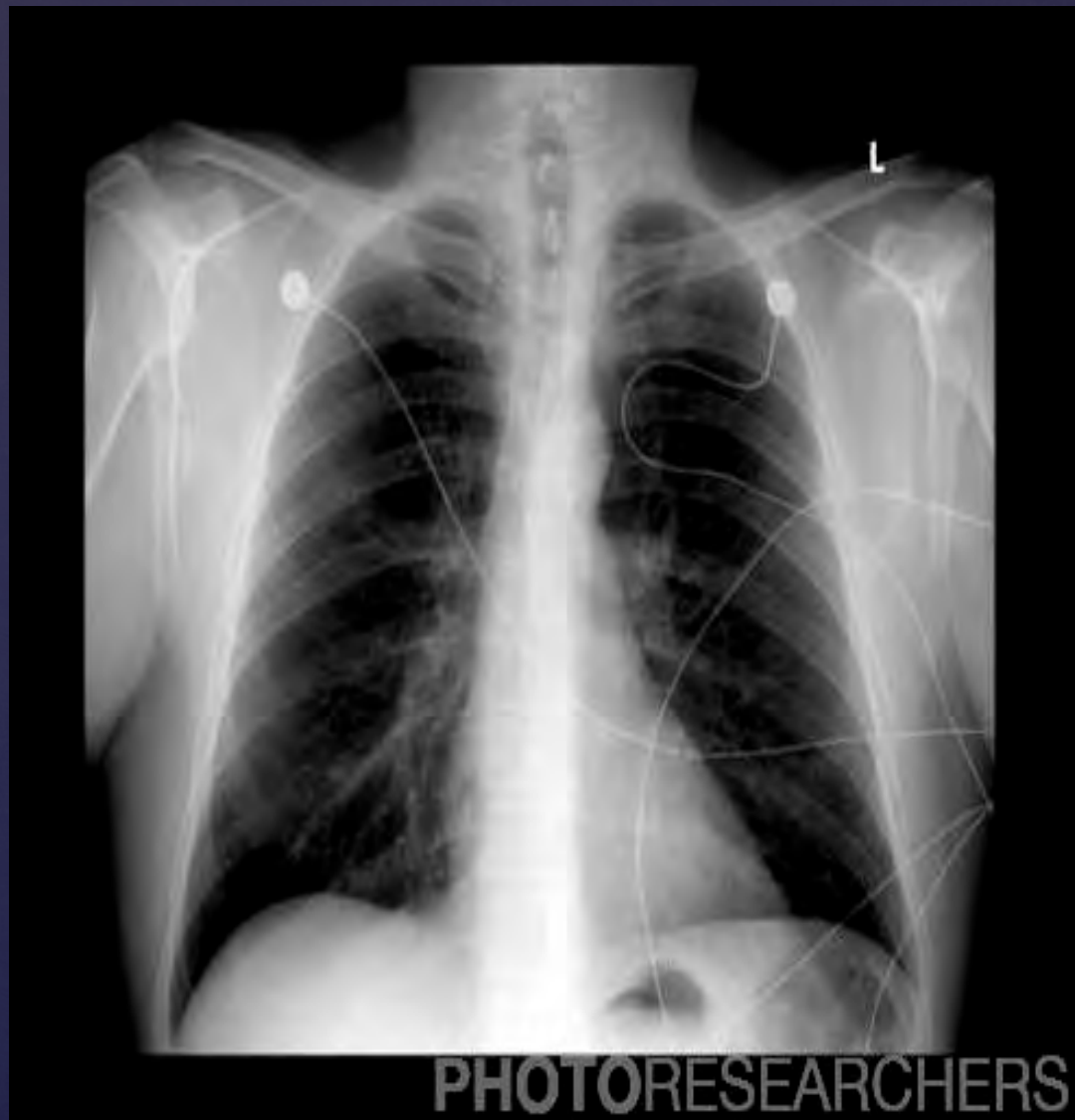
Can provide a confident diagnosis 25% of cases

A Normal CXR


Manubrium
Superior vena cava
Right main bronchus
Horizontal fissure
Right atrium
Oblique fissure
Inferior vena cava
Diaphragm / Liver
Aortic arch
Pulmonary trunk
Left main bronchus
Left atrium
Left ventricle
Oblique fissure
Diaphragm
Left costo-phrenic angle
Gastric bubble

Evaluating a CXR

- Airways
- Bones
- Cardiac Silhouette
- Diaphragm
- Esophagus
- Fissures
- Gastric Bubble
- Hila



Abnormal CXR with ILD

Alveolar Filling

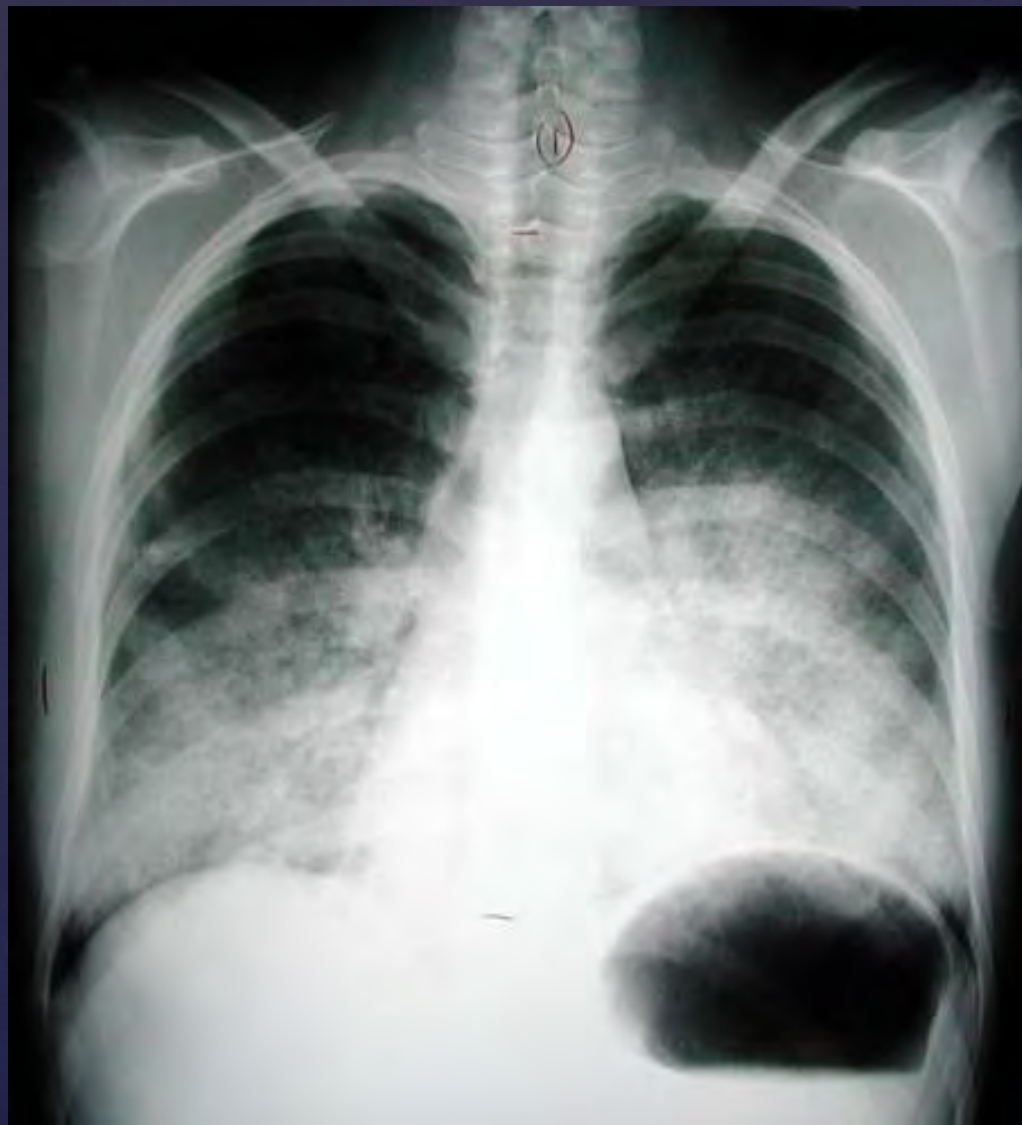
Air-bronchograms

Acinar rosettes (rose)

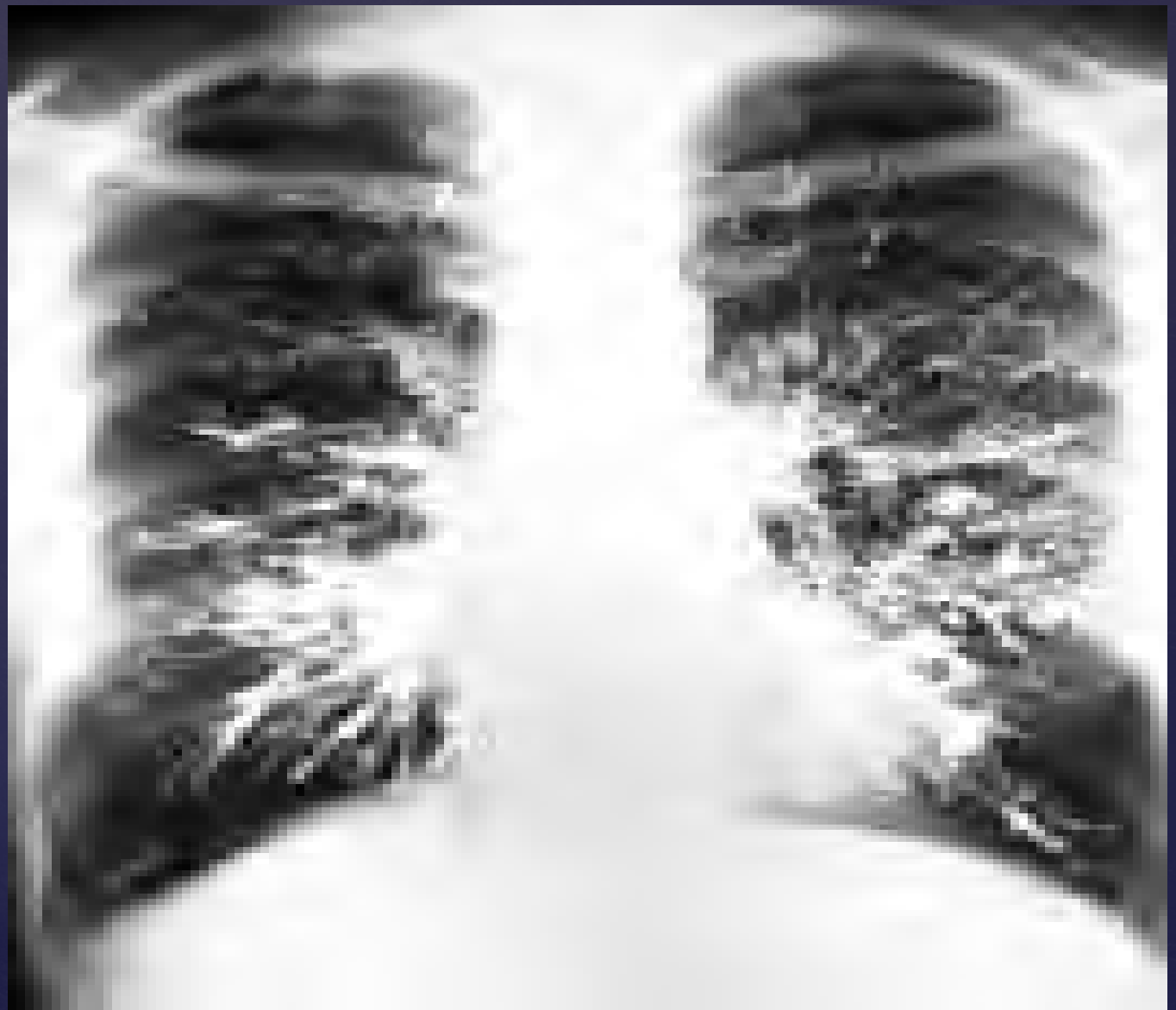
Diffuse consolidation

Nodule/unclear border

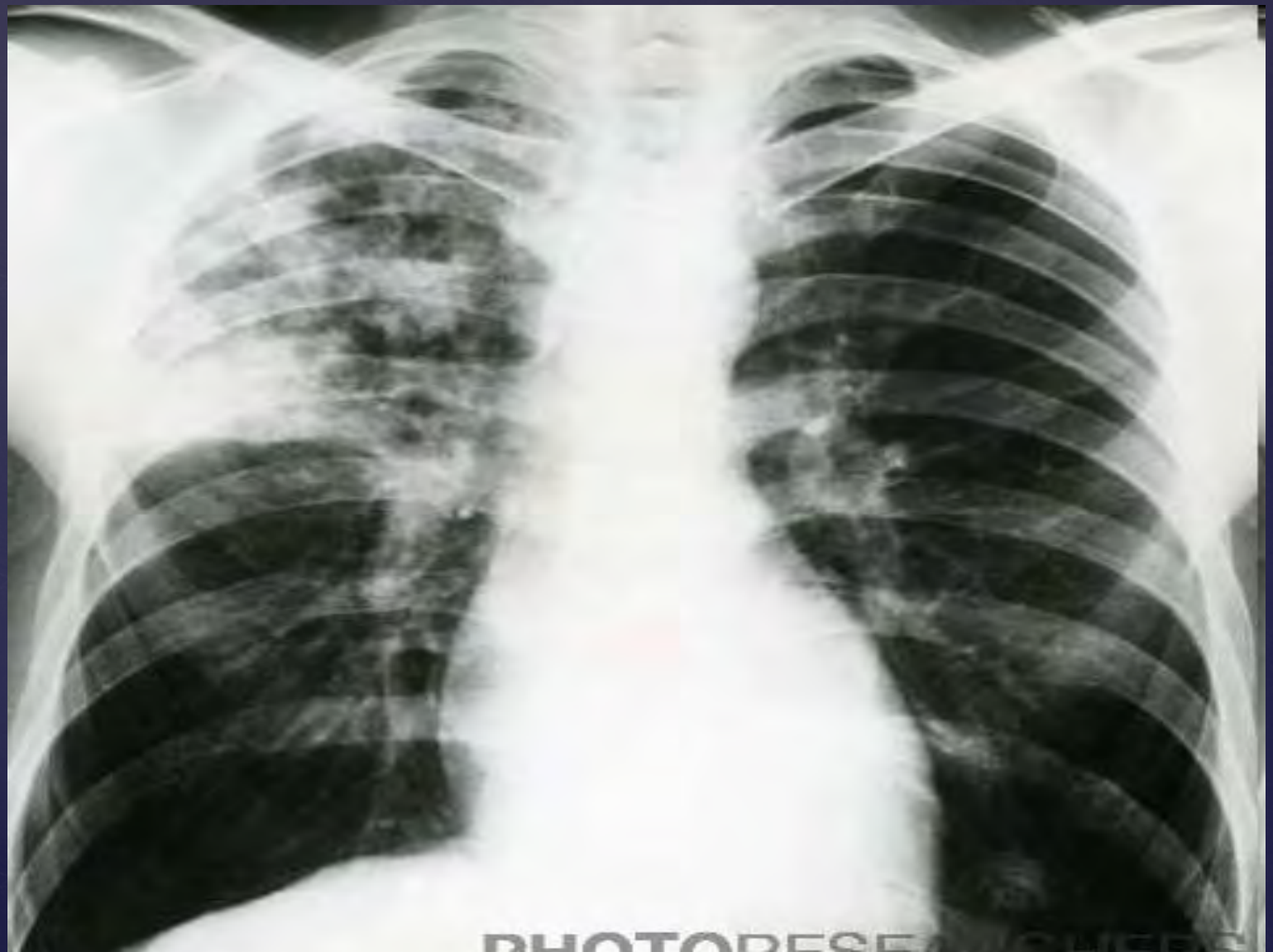
Silhouetting



Bronchiectasis

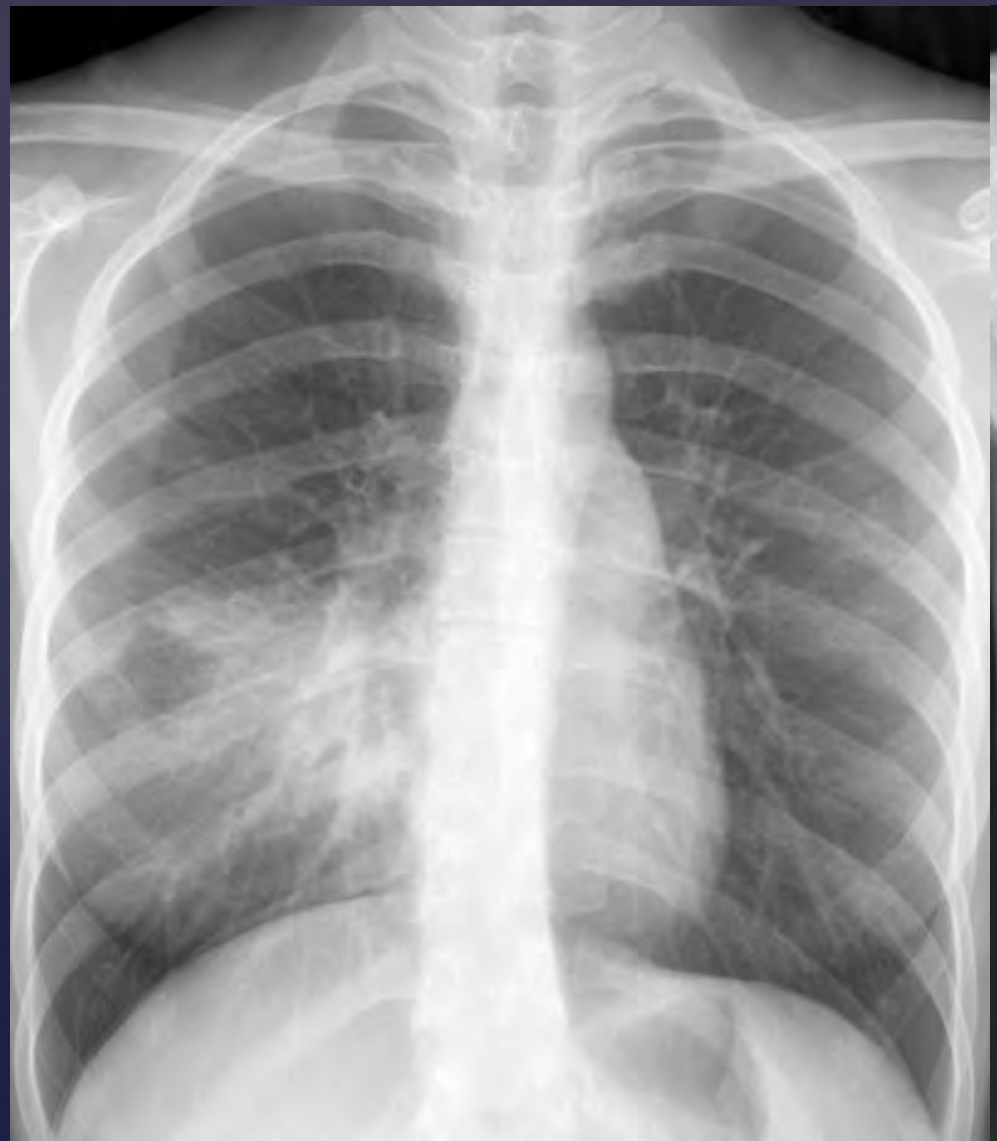


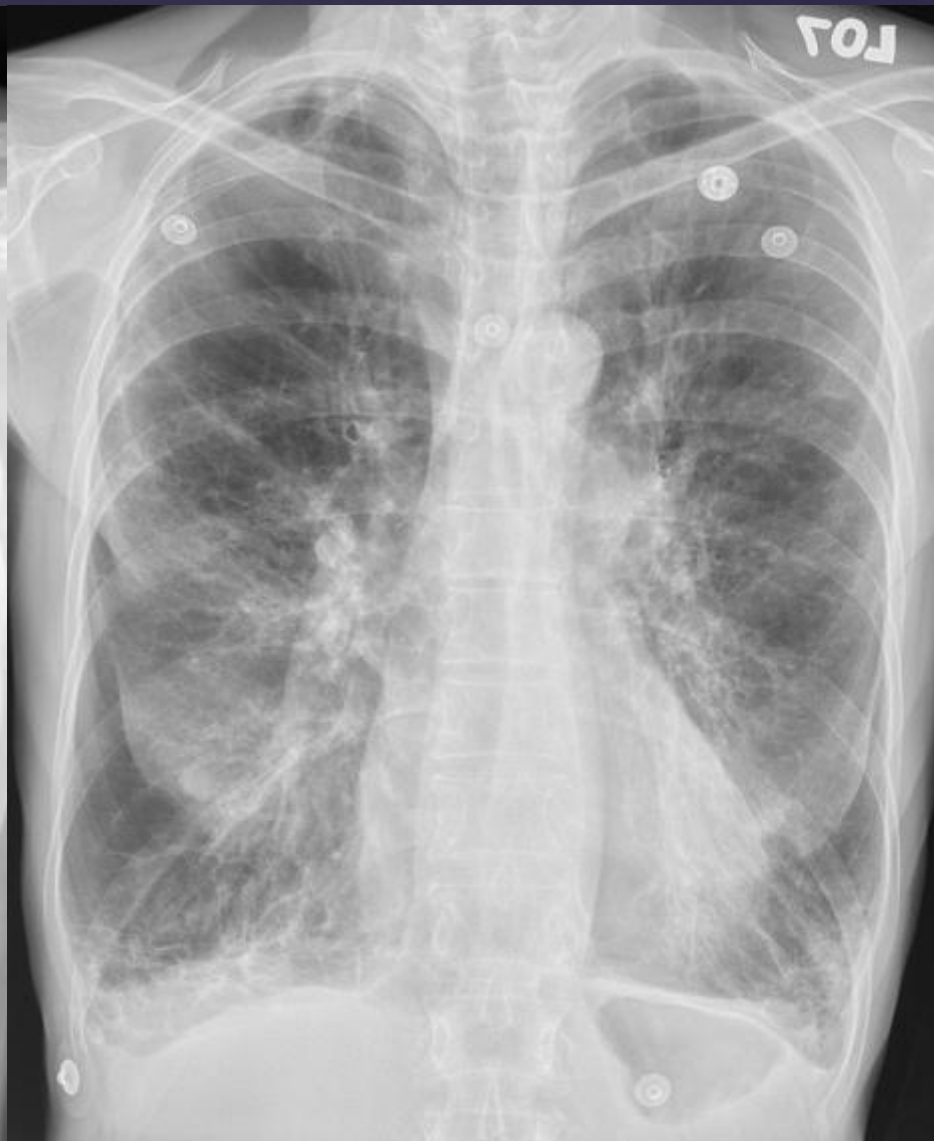
TB and CF: Upper Lobe Disease



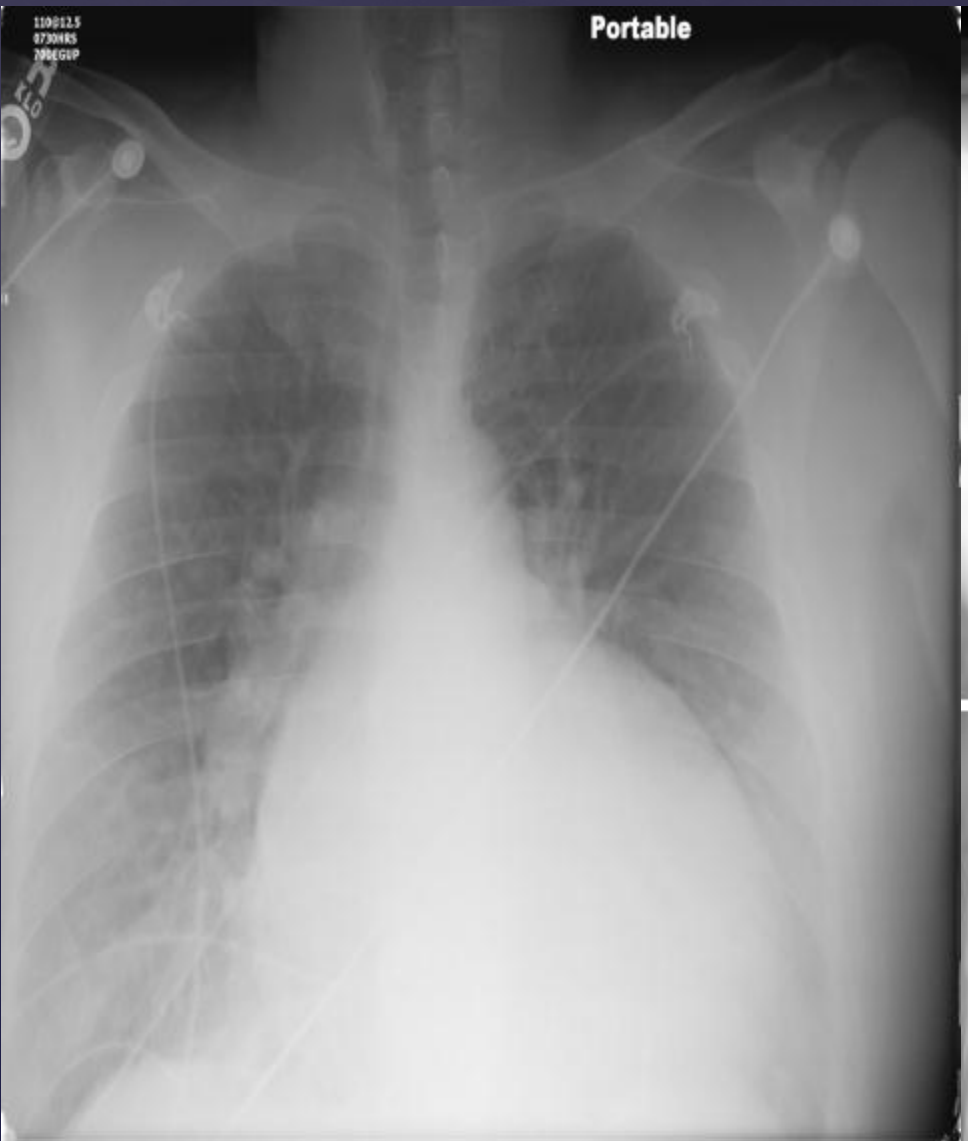
RML PNA

COPD

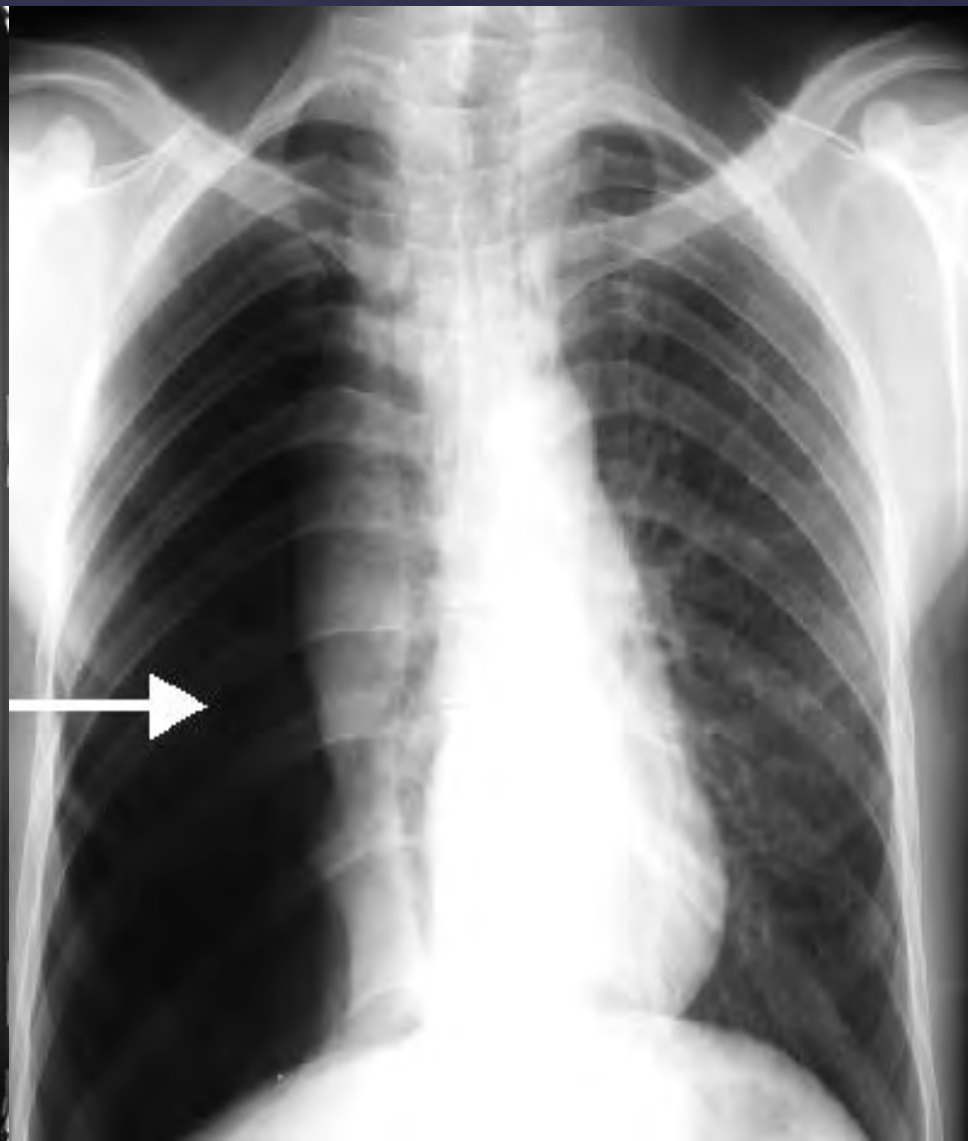




CHF



Pneumothorax



HRCT Findings with ILD

High-resolution CT findings of pulmonary disease: increased and decreased lung opacity

HRCT finding	Further pattern subclassification	Diseases frequently implicated
Increased lung capacity		
Nodules	Centrilobular, perilymphatic, random	Bronchiolitis, sarcoidosis, Hematogenously disseminated infection
Linear abnormalities	Interlobular septal thickening, parenchymal bands, subpleural lines	Pulmonary edema, lymphangitic carcinomatosis
Reticular abnormalities	Coarse or fine reticulation, intralobular interstitial thickening	Idiopathic interstitial pneumonias, pneumoconioses
Ground-glass opacity	Must be based on clinical history and associated scan findings	Opportunistic infection, idiopathic interstitial pneumonia, pulmonary alveolar proteinosis
Consolidation	Must be based on clinical history and associated scan findings	Pneumonia, cryptogenic organizing pneumonia, pulmonary hemorrhage
Decreased lung capacity		
Areas of decreased attenuation with walls (cysts or ccystlike appearance)	Cyst shape, distribution, wall thickness, pattern of organization	Langerhans' cell histiocytosis, lymphangioleiomyomatosis, bronchiectasis, paraseptal emphysema, idiopathic interstitial pneumonias
Areas of decreased attenuation without walls	Emphysema, mosaic perfusion	Centrilobular or panlobular emphysema, diseases affecting small airways

Evaluating an HRCT

Interstitial Markings:

- Linear: 2-6cm long (ladder); ex: Kerley A and B Lines
- Reticular (spider web/giraffe formation)
- Nodular (size matters): Miliary/Acinar/Interstitial

Location:

- Upper/lower
- Periphery/Central/Scattered

Patterns:

- IPF/Mosaic/Ground Glass Opacities
- Crazy Paving/Consolidation

Evaluating a Chest HRCT

Masses: Malignancy, granulomas, congenital abnormalities; infection/abscess, inflammation, calcification

Opacities: Hemorrhage, exudate, transudate, malignancy

Interstitial disease:

- Linear:
  - Kerley lines (inflammation, fibrosis and edema)
  - LIFE: lymphangitic spread of malignancy, inflammation, fibrosis and edema
- Nodular:
  - Small, sharp, numerous, evenly distributed (granulomas, pneumoconiosis, hematogenous spread of malignancy

Evaluating a Chest HRCT

Vascular Changes

Increased/decreased perfusion altering diameter of pulmonary vessels

Examples: Congestion; Emphysema; Arterial HTN; Thromboembolism, Shunting, Bronchial circulation, Lymphangitic carcinoma

Evaluating a Chest HRCT

Bronchial obstruction or wall thickening

Complete Obstruction: opacity with decreased volume of lung distant to obstruction

Ex: Neoplasms, granulomas, mucous plugs, foreign bodies

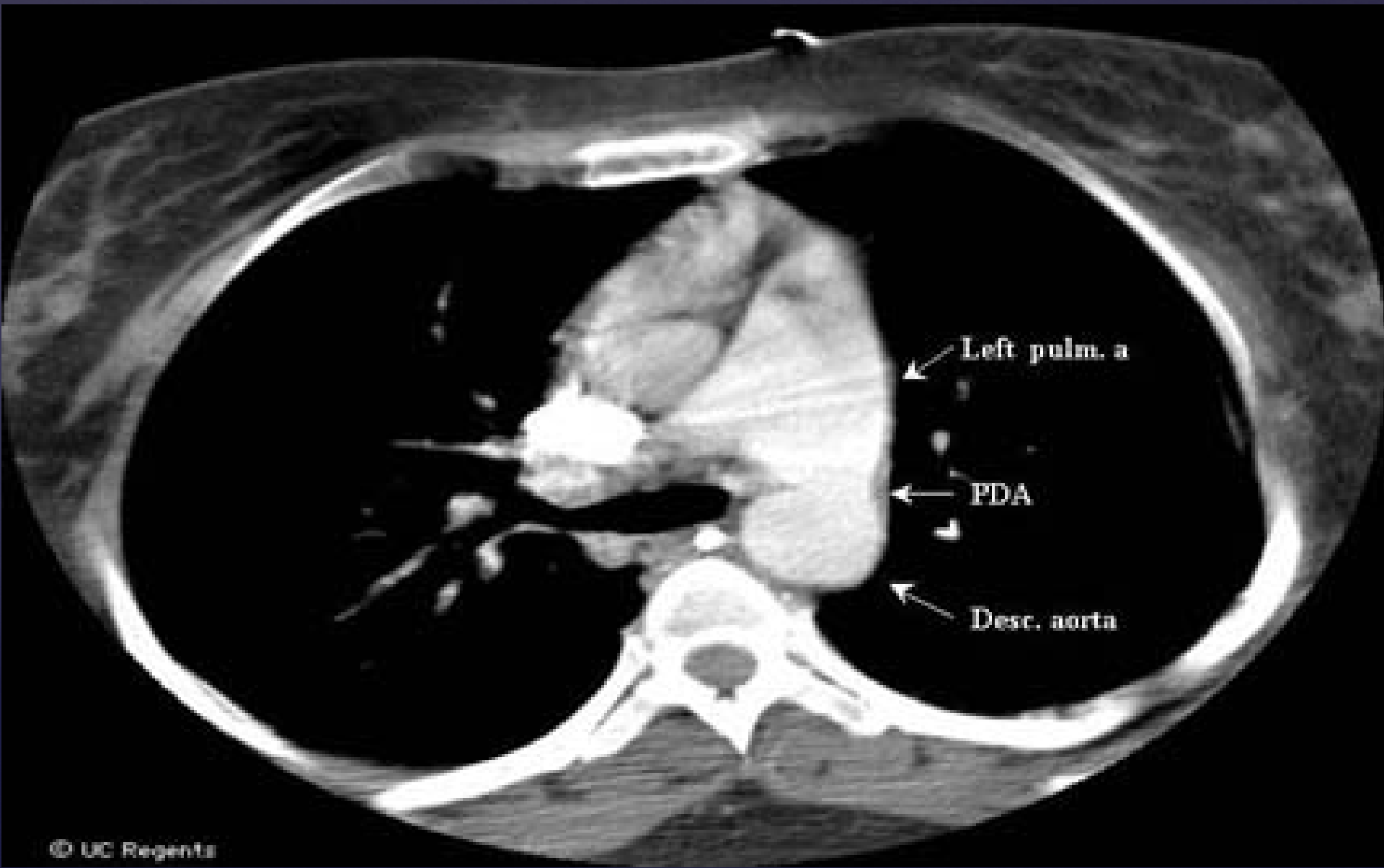
Partial Obstruction: lucency and increased volume by air trapping

Ex: COPD, cysts, blebs, pneumatoceles

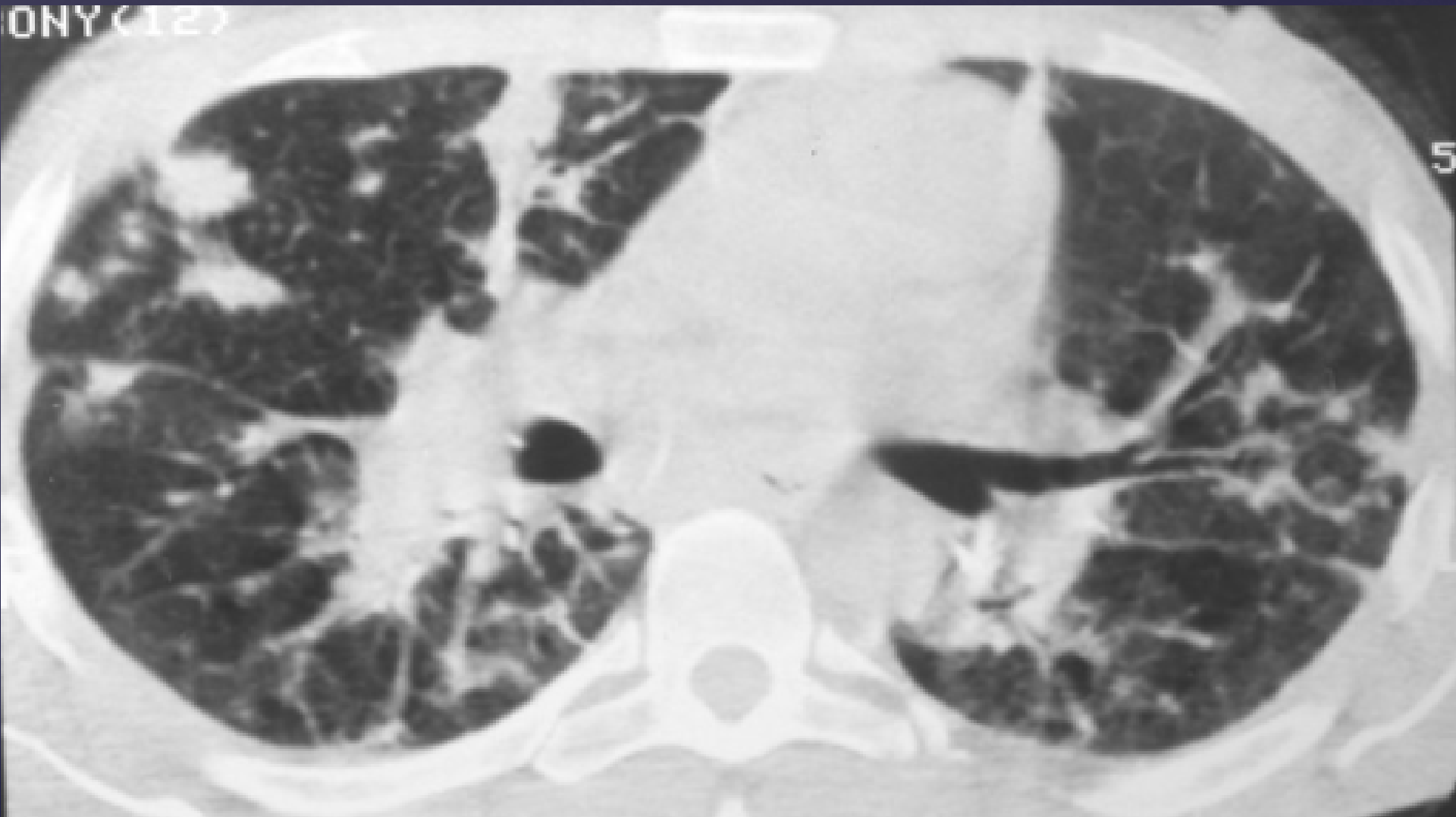
Wall Thickening: tram tracks, central cystic spaces or circles

Ex: Bronchiectasis (destruction with cyst formation), chronic bronchitis

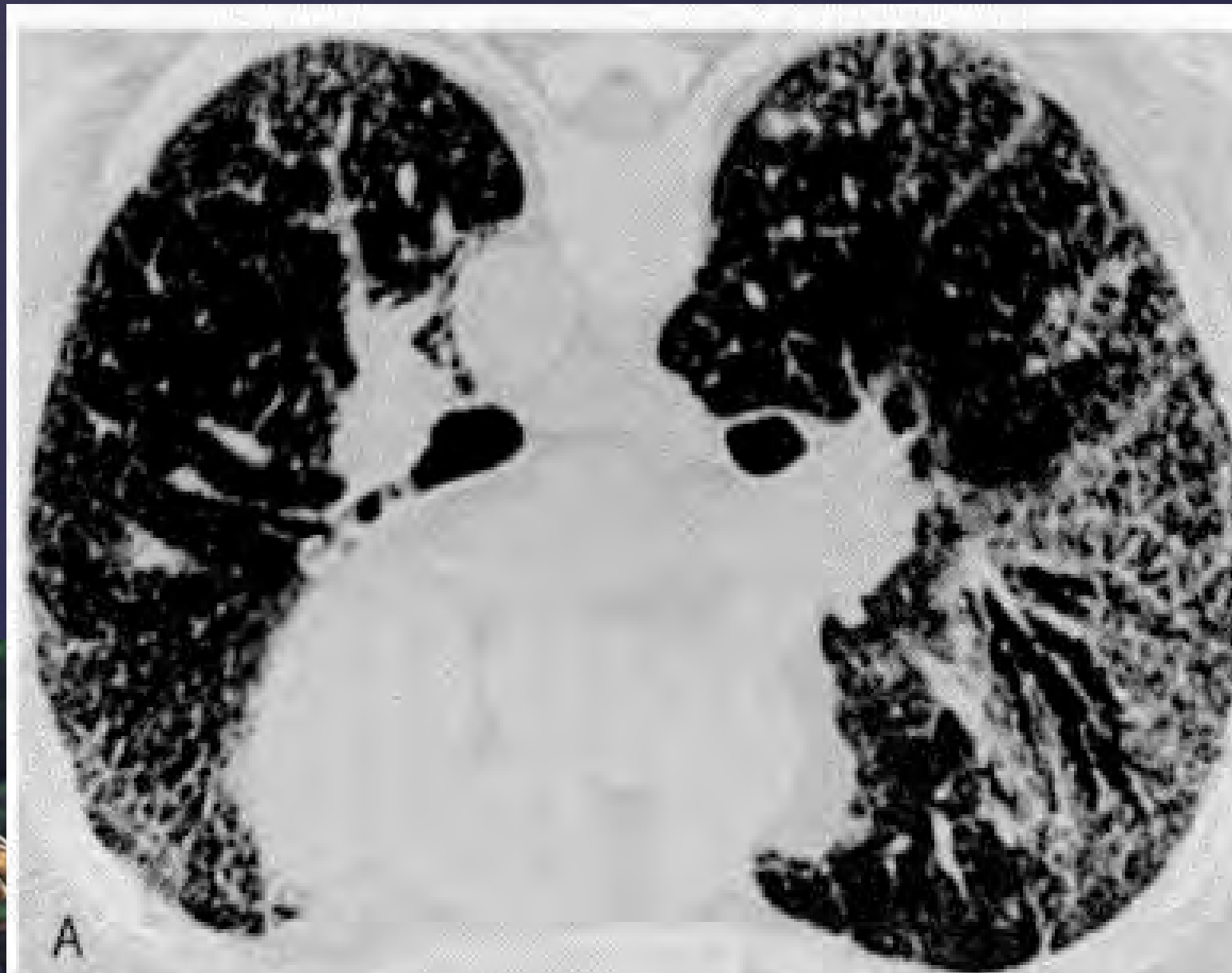
Normal CT



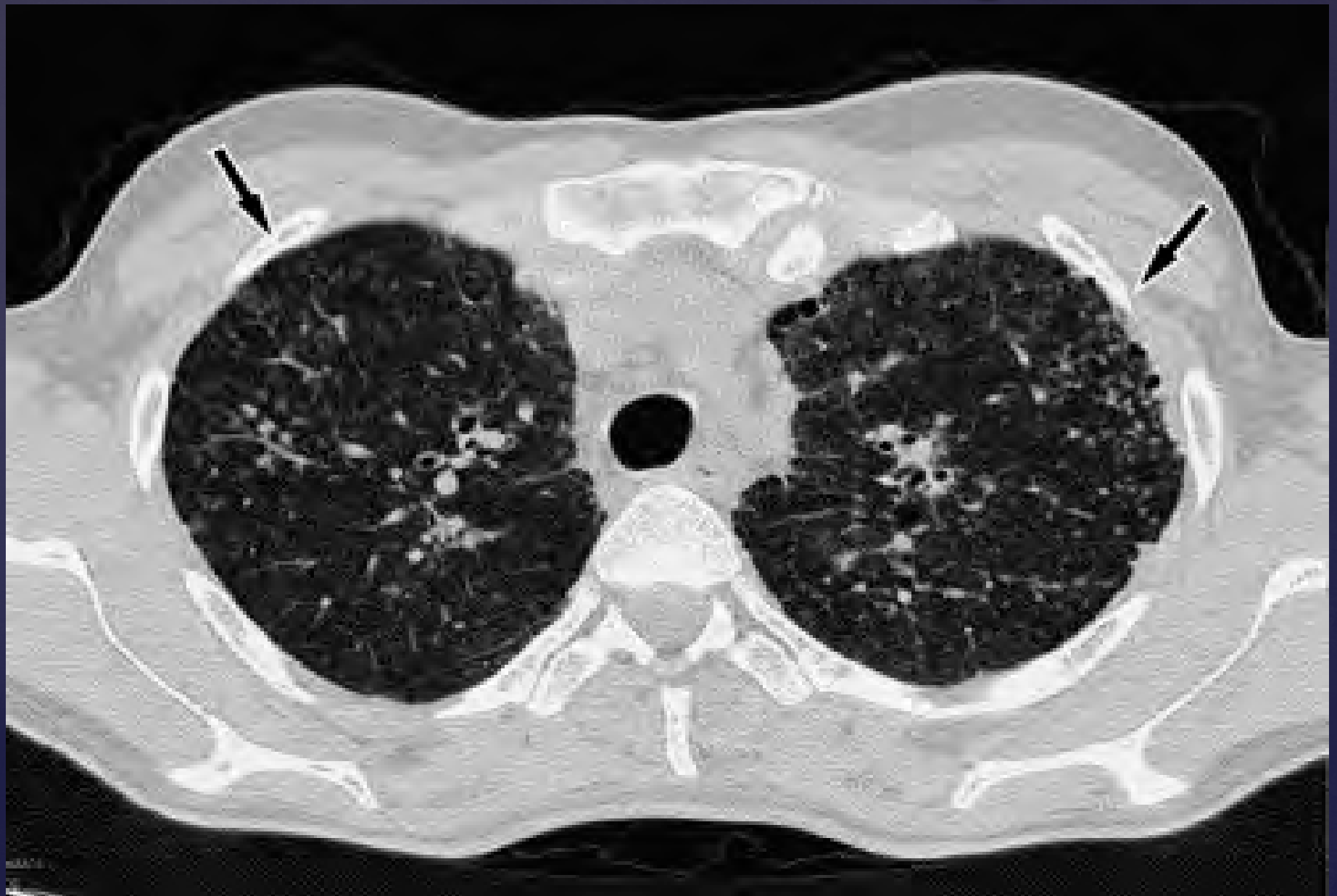
Linear Markings: Septal Thickening



Reticular Markings



Nodular Markings



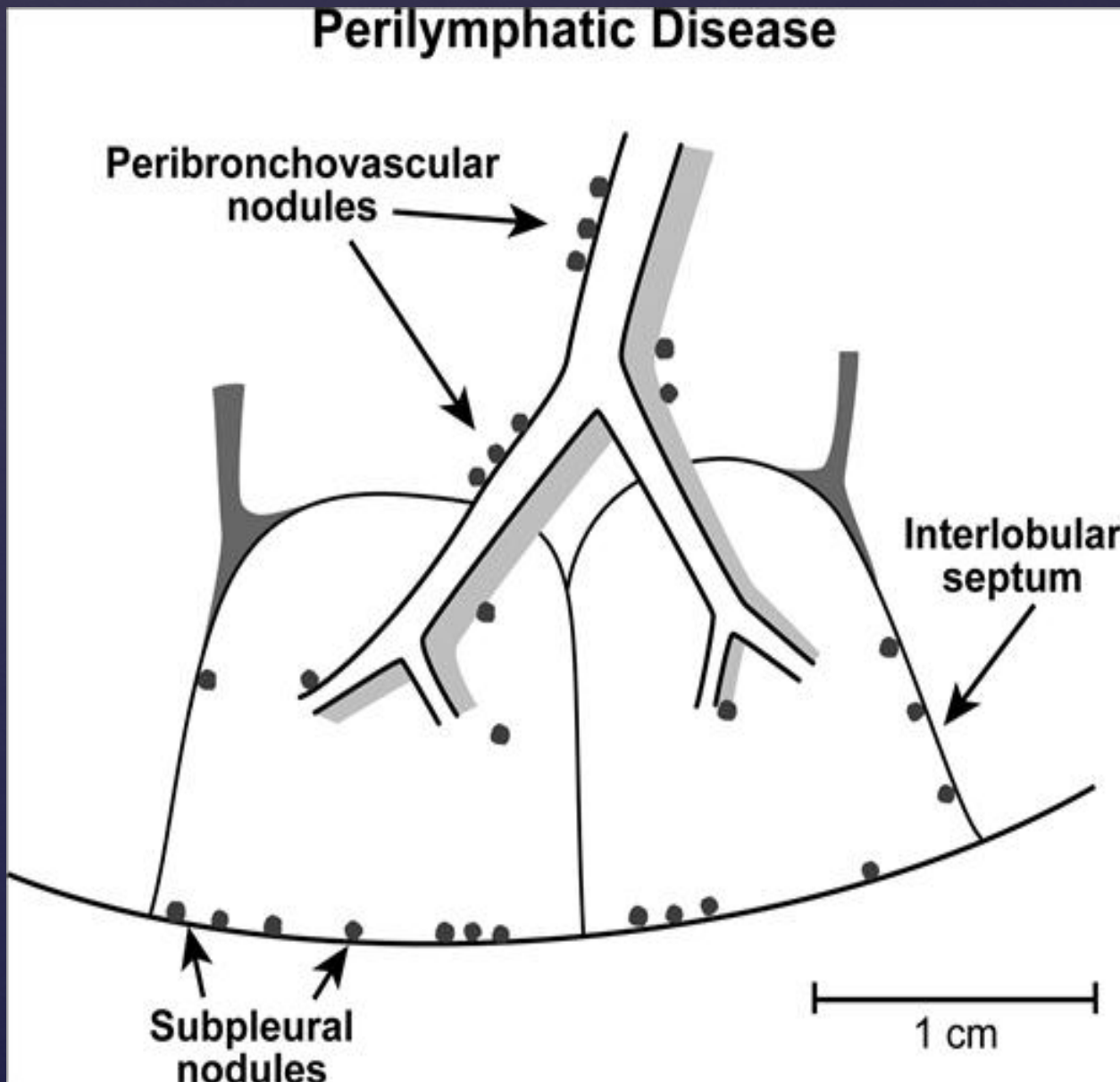
Location is Key

Central

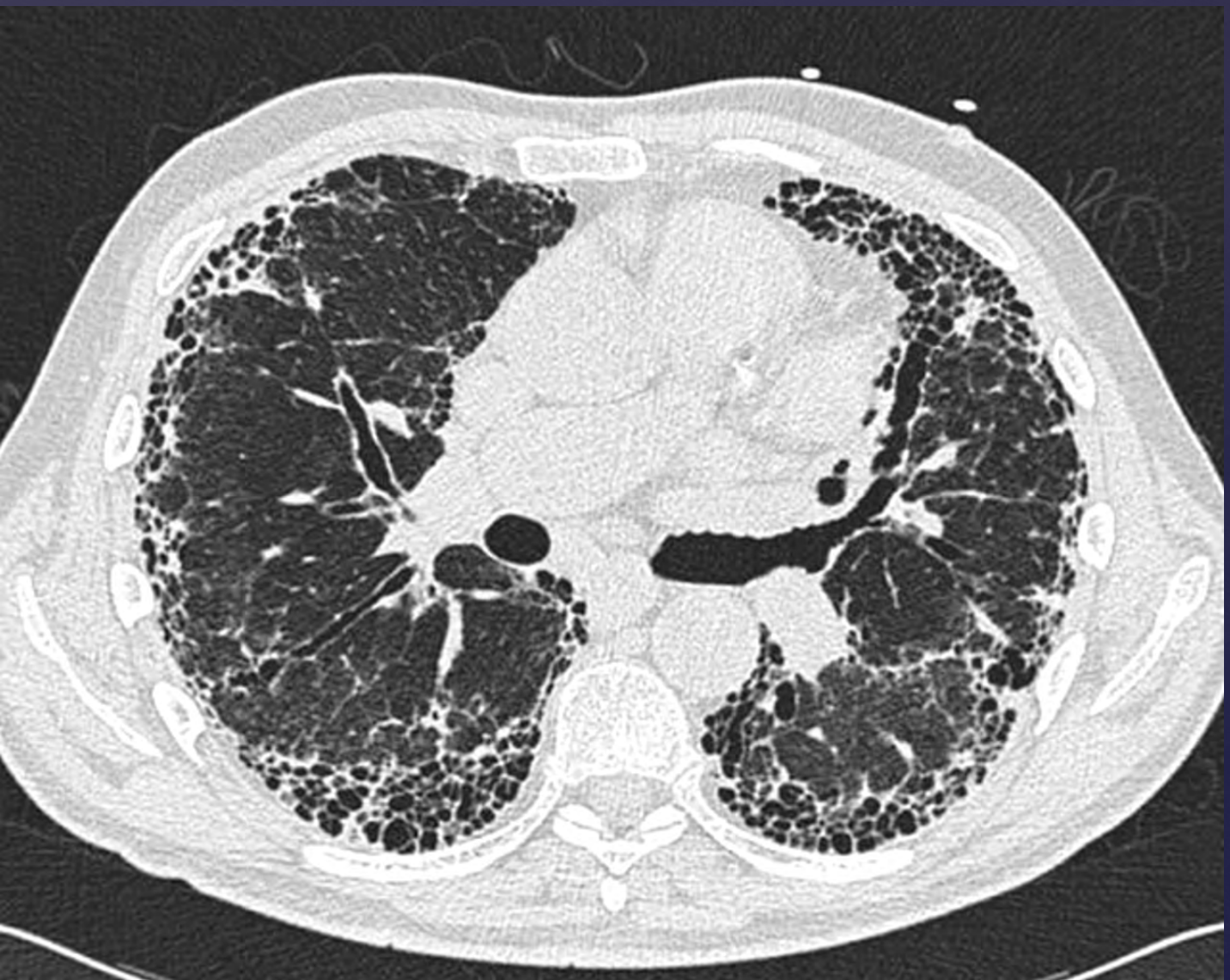
Lobular

Scattered

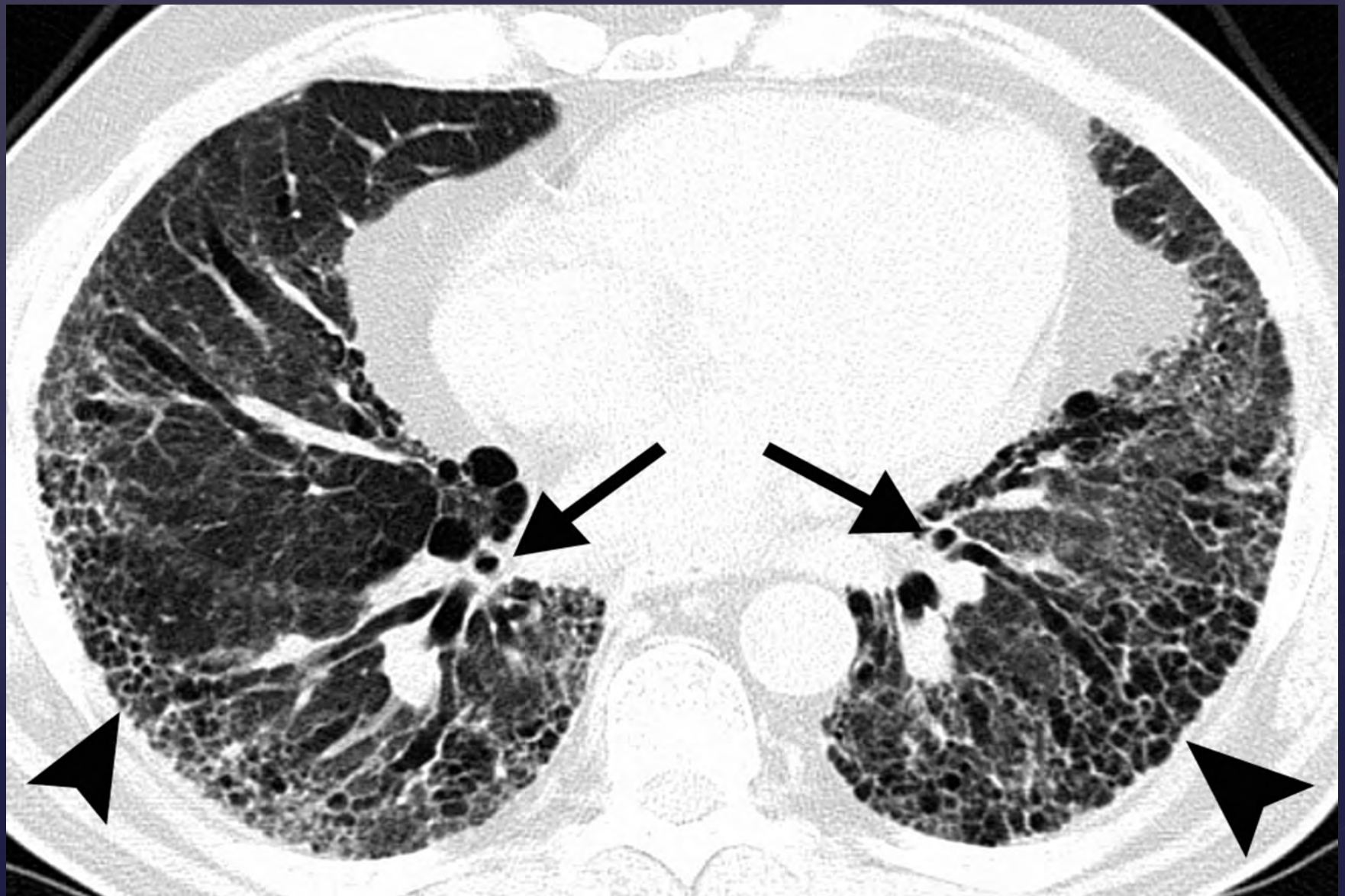
Perilymphatic



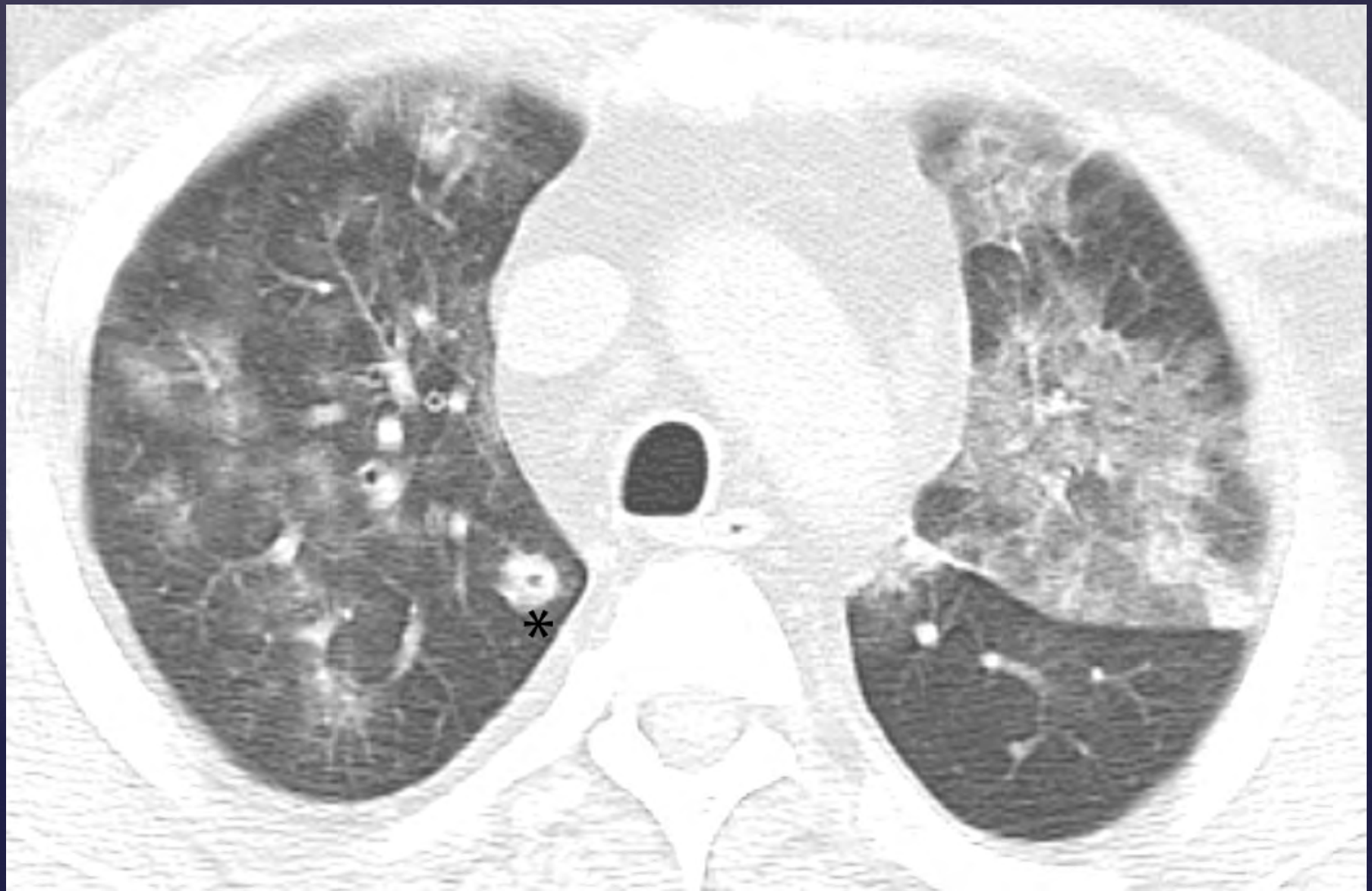
Fibrosis Pattern: Sub-pleural Honeycombing



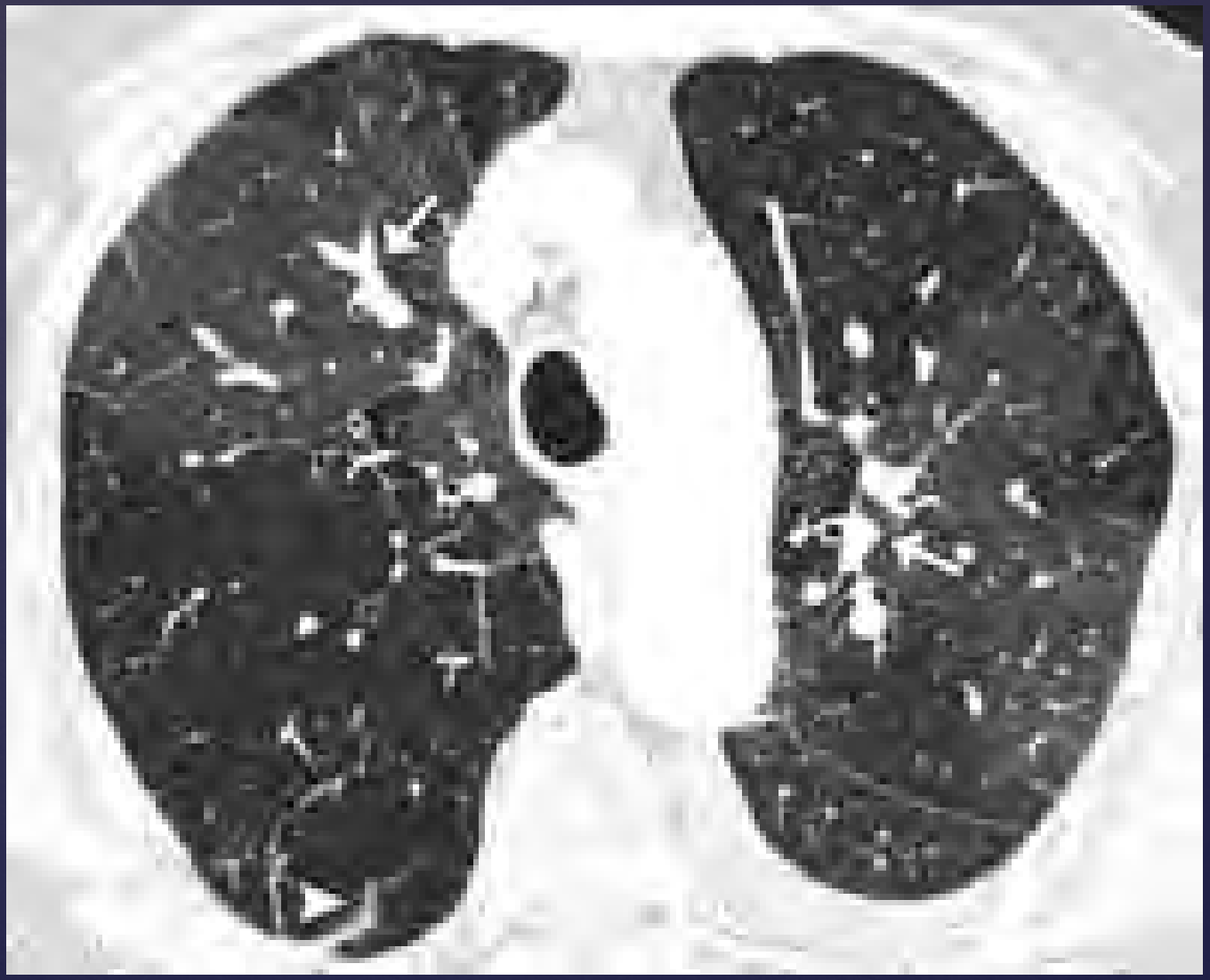
Traction Bronchiectasis Pattern: lung parenchymal distortion



Ground Glass Opacities Pattern: Inflammatory Response/Fog like



Mosaic Attenuation Pattern: Air Trapping



HRCT only on inspiration/expiration views; Evaluate on expiratory view

Pulmonary Function Testing

Demographics: Ht/Wt/Age/Sex

Restrictive vs Obstructive
- Normal Values >80%
- Mild 60-80%
- Moderate 40-60%
- Severe <40%

Criteria
- Volume and Percentage
- FEV1, FVC, FEF 25-75, DLCO Obstructive

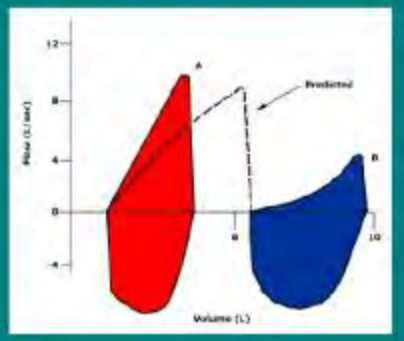
Bronchodilator affect: >12% or 200ml r/t asthma

PFT with Loops/Lung Volumes

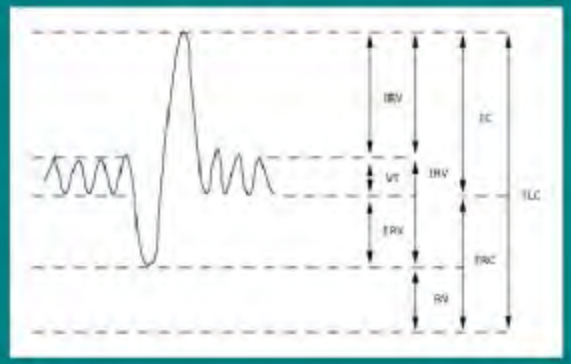
KNUDSON PREDICTEDS

		Predicted Value	Observed Pre	%Pred
SPIROMETRY				
FVC	L	2.75	1.52*	55
FEV1	L	2.17	1.14*	52
FEV1/FVC	%	77	75	97
FEF25-75	L/S	2.13	.85*	39
PEFR	L/S	5.41	3.57*	65
FET	Sec		6.13	
FIVC	L		1.43	
PIFR	L/S	3.6	2.1 *	58
LUNG VOLUMES				
SVC	L	2.75	1.57*	57
IC	L	2.06	1.16*	56
ERV	L	.69	.41*	59
FRC	L	2.79	1.88	67
RV	L	2.1	1.47	70
TLC	L	4.85	3.04	62
RV/TLC	%	43	48	111
DIFFUSION				
DLCO UNC		20.32	9.84*	48
DLCO CORR		20.32	9.73*	47
HB 15.0				
VA @BTPS		5.49	2.78*	50
DL/VA		5.04	3.5 *	69

Spirometry



Lung Volumes



Six Minute Walk

- O2 Sats
  - Baseline/Exercise/Recovery
  - Need for supplemental O2 sats <88%
- Distance Walked
- DOE (1-4)

Pulmonary Hypertension Findings

12 Lead EKG Abnormalities:

P wave: greater than or equal to 2.5 mm in leads II, III and aVF

RV Strain: ST depression in the right precordial leads

Echo Abnormalities:

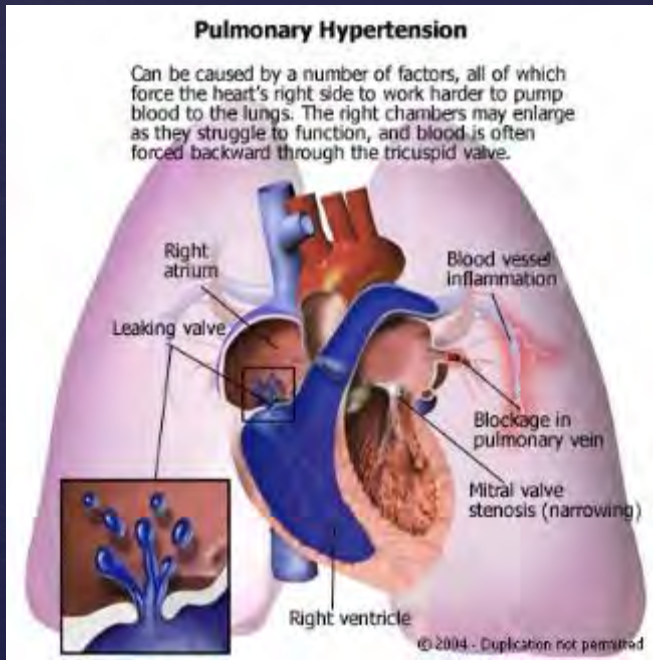
Thickening of the right ventricle

Mild to severe MR

RVSP 23mmHg (normal)

RA/RV size

LV Function: 60% EF (normal)



Medications Causing ILD

Antibiotics
- Nitrofurantoin, acute and chronic
- Sulfasalazine
- Minocycline
- Ethambutol

Anti-inflammatory agents
- Gold
- Penicillamine
- Nonsteroidal antiinflammatory agents

Anti-arrhythmic agents
- Tocainide
- Amiodarone

Chemotherapeutic agents
- Antibiotics
  - Bleomycin sulfate
  - Mitomycin C
- Alkylating agents
  - Busulfan
  - Cyclophosphamide
  - Chlorambucil
  - Melphalan
  - Procarbazine hydrochloride
- Antimetabolites
  - Azathioprine
  - Cytosine arabinoside
  - Methotrexate
- Nitrosoureas
  - BCNU (carmustine)
  - CCNU (lomustine)
  - Methyl-CCNU (semustine)
- Other
  - Etoposide (VP-16)
  - Paclitaxel
  - Docetaxel
  - Thalidomide
  - Nilutamide
  - Alpha interferon
  - Gefitinib

Drug-induced systemic lupus erythematosus
- Procainamide hydrochloride
- Isoniazid
- Hydralazine hydrochloride
- The hydantoins
- Penicillamine

Illicit drugs
- Heroin
- Cocaine
- Methadone hydrochloride
- Propoxyphene hydrochloride (Darvon)
- Talc

Miscellaneous
- Oxygen
- Drugs inducing pulmonary infiltrates and eosinophilia
- Radiation
- L-tryptophan
- Bromocriptine
- Bacille Calmette-Guerin (BCG)

Genetically Susceptible

- Multiple or aggressive underlying illness immunocompromised

Genetically Pre-disposition

- May present 10yrs earlier in offspring

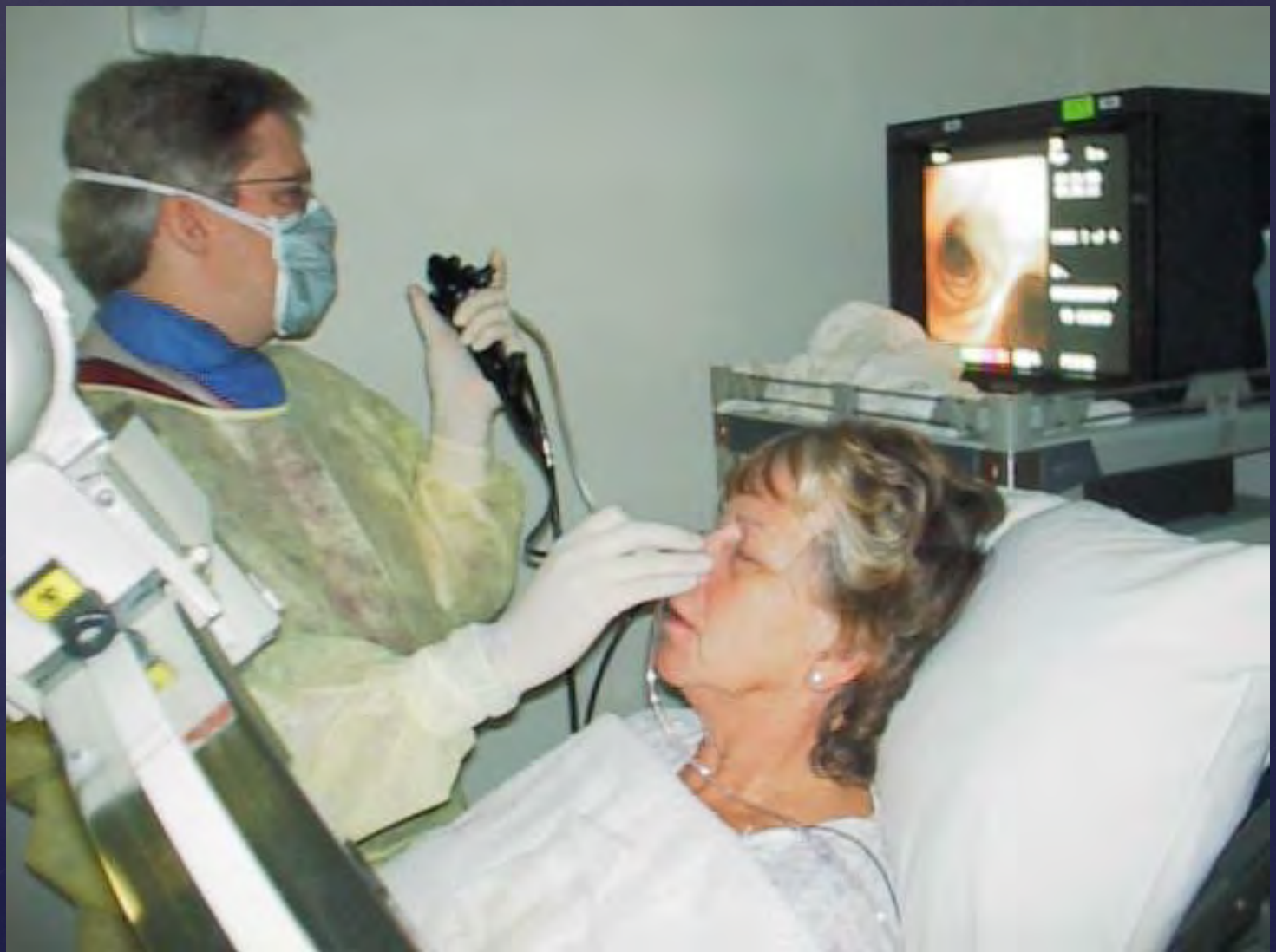
Autosomal dominant

Family His

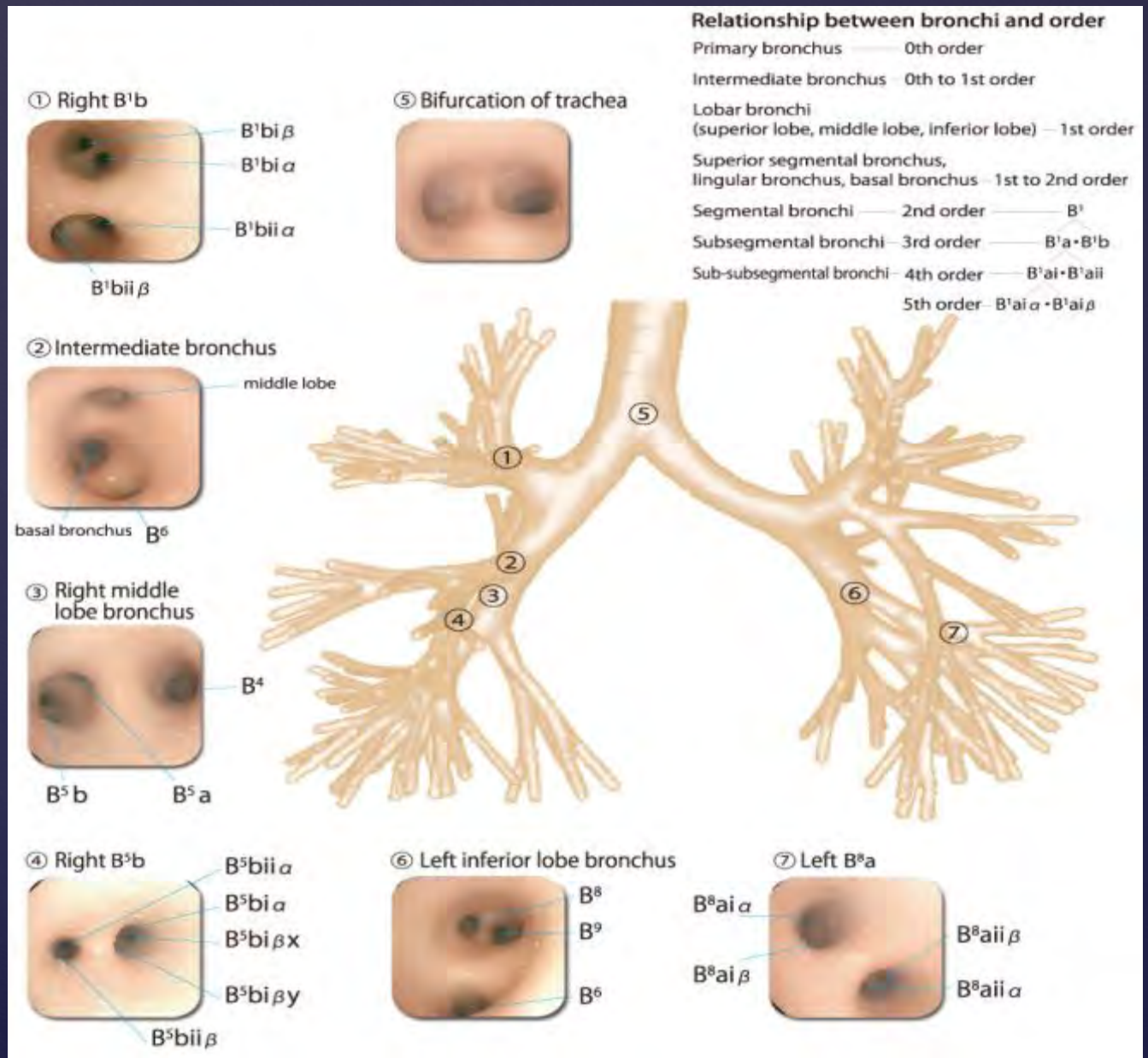
Labs and Pathology

- CBC
- BMP
- LFT
- RF, ANA, ANCA, Hyperse
  panel, anti-GBM
- Not done: CRP; ESR (not s
  enough)

Bronchoscopy: Lavage, Biopsy or Both



Lung Biopsy


Relationship between bronchi and order
Primary bronchus — 0th order
Intermediate bronchus — 0th to 1st order
Lobar bronchi (superior lobe, middle lobe, inferior lobe) — 1st order
Superior segmental bronchus, lingular bronchus, basal bronchus — 1st to 2nd order
Segmental bronchi — 2nd order — B¹
Subsegmental bronchi — 3rd order — B¹a・B¹b
Sub-subsegmental bronchi — 4th order — B¹ai・B¹aii
5th order — B¹aiα・B¹aiβ
① Right B¹b
B¹biβ
B¹biα
B¹biiα
B¹biiβ
⑤ Bifurcation of trachea
② Intermediate bronchus
middle lobe
basal bronchus
B⁶
③ Right middle lobe bronchus
B⁴
B⁵b
B⁵a
④ Right B⁵b
B⁵biiα
B⁵biα
B⁵biβx
B⁵biβy
B⁵biiβ
⑥ Left inferior lobe bronchus
B⁸
B⁹
B⁶
⑦ Left B⁸a
B⁸aiα
B⁸aiβ
B⁸aiiβ
B⁸aiiα
1
2
3
4
5
6
7

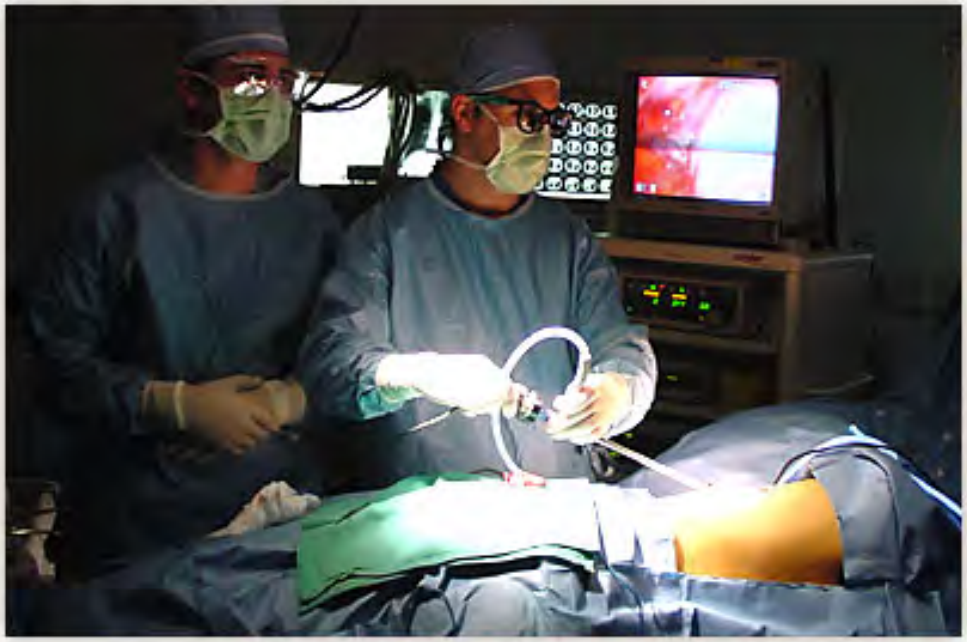
Lung Biopsy

Purpose

- Pathology for diagnosis
- Need to obtain multiple biopsies (5-12 sites) from RML or area in question

Types:

- VATS: video assisted thoroscopic
- Open lung Biopsy



ILD Exacerbation: Admit

10% drop in FEV1
Increased productive cough
Fevers/chills
N/V/D or significant constipation/SBO
Hemoptysis
Increased SOB with h/o ABPA
Drop in weight

ILD Hospital Admission

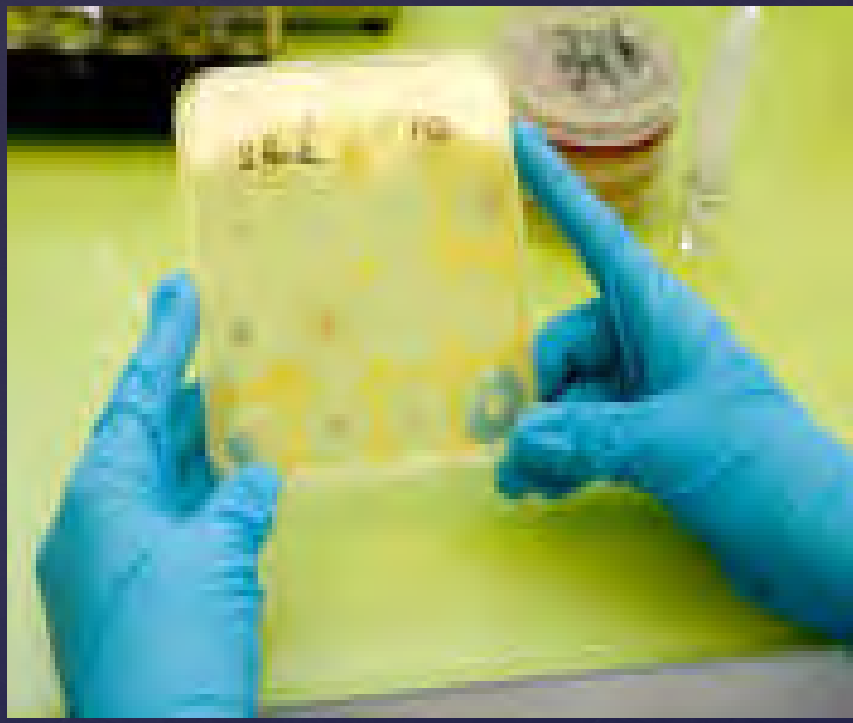
Meds
- Continue with daily treatments
- Antibiotics selected
  - based on allergy panel, MIC, thearaputic coverage and last sputum culture

Labs
- CBC, BMP, LFT, Coags, IgE, A1C

Diagnostics:
- 2 View CXR
- SC, AFB and fungal cx
- KUB, US, Chest or Sinus CT – will order prn

Respiratory Care
- CPT/Vest/IPV/G5 q4hr W/A

Antibiotic Selection



Typical Organisms

- MSSA/MRSA
- Stenotrophomonas
- B Cepecia
- Achromobacter

Microbiology Testing on Sputum Cultures:

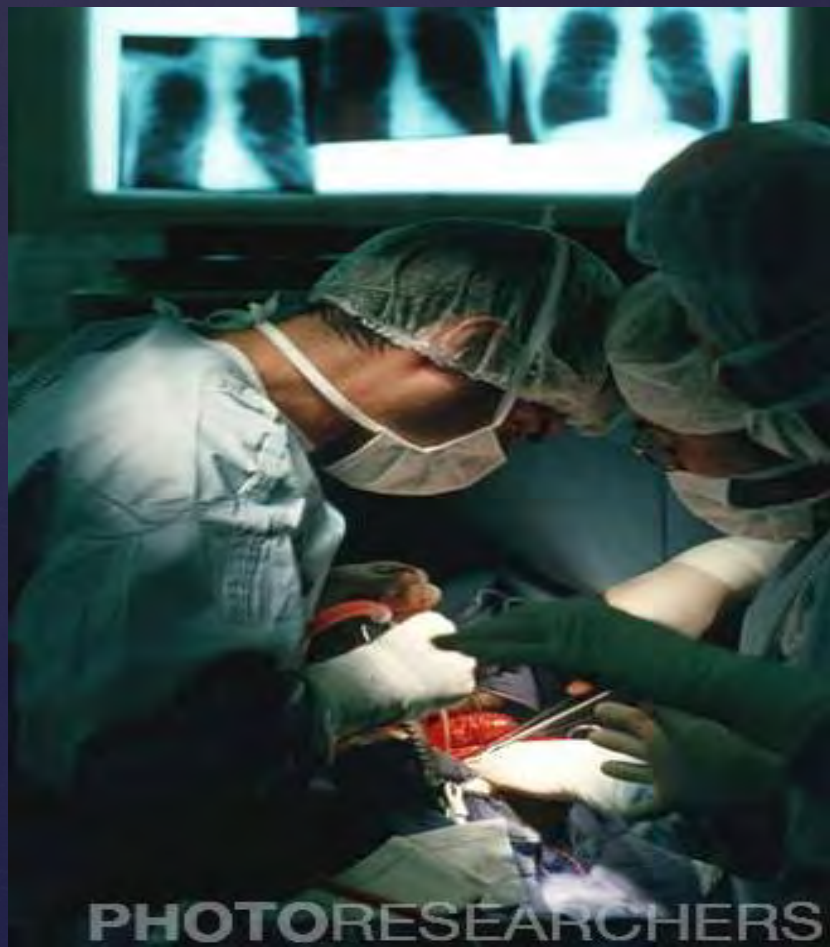
- Kirby Bower
- E-Test

Long Term Management

Managing ADLs
Exercise
Nutrition vs Weight Loss
Lung Transplantation
Palliative Care: Death and Dying

Work-Up for Transplant

- Referral to Transplant Team
- CT Echo PFT Angio
- CMP/CBC, Virology, Antibody screens
- Psych Evaluation
- Family Support
- Financial Authorization



THE END


Thank you