The ABC's of ILD

Classification

- Clinical
  - Idiopathic Disorders
    - Pulmonary Fibrosis
    - NSIP
    - COP
    - AIP
  - Sarcoidosis
  - Connective Tissue Disease
  - Drug-Induced
  - Occupational/Environmental
  - Pulmonary Alveolar Proteinosis
  - Cystic Lung Disease
    - Pulmonary Langerhans Cell Histiocytosis
    - LAM
    - LIP
- Pathologic
  - Diffuse Alveolar Damage
  - Organizing Pneumonia
  - Desquamative Interstitial Pneumonia
  - Nonspecific Interstitial Pneumonia
  - Usual Interstitial Pneumonia
  - Lymphocytic Interstitial Pneumonia
  - Eosinophilc Pneumonia
  - Alveolar Proteinosis

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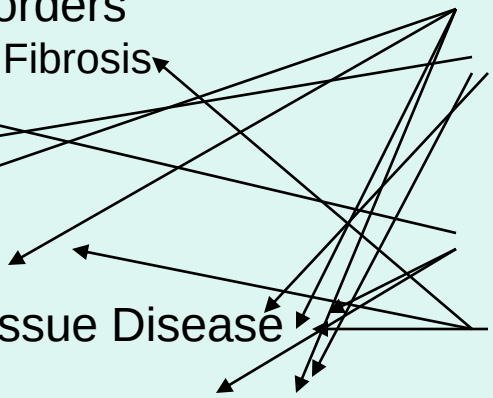

- **Pathologic**
  - Diffuse Alveolar Damage
  - Organizing Pneumonia
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  - Lymphocytic Interstitial Pneumonia
  - Alveolar Proteinosis

First Step in Diagnosing ILD

TAKE A HISTORY!

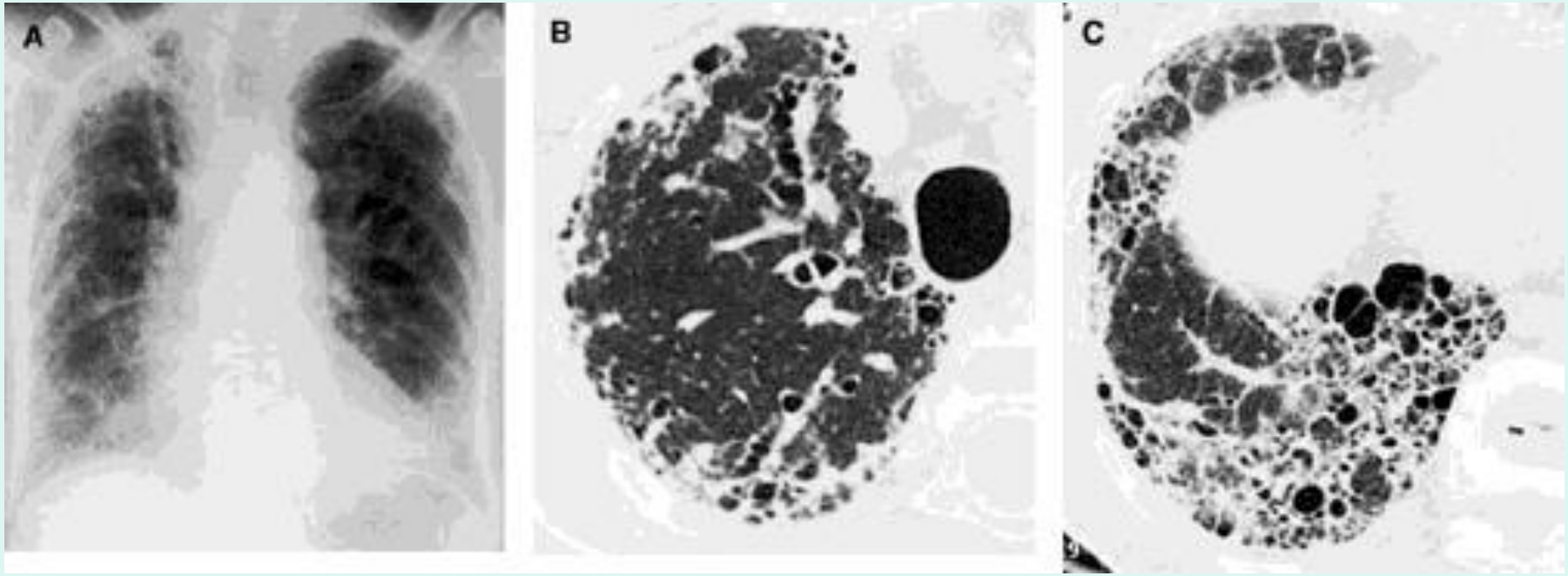
Clinical Approach to ILD

- Demographics
  - Age
  - Gender
- Duration of Illness
- Smoking History
- Family History
- Current and prior medications
- Occupational History
- Environmental History

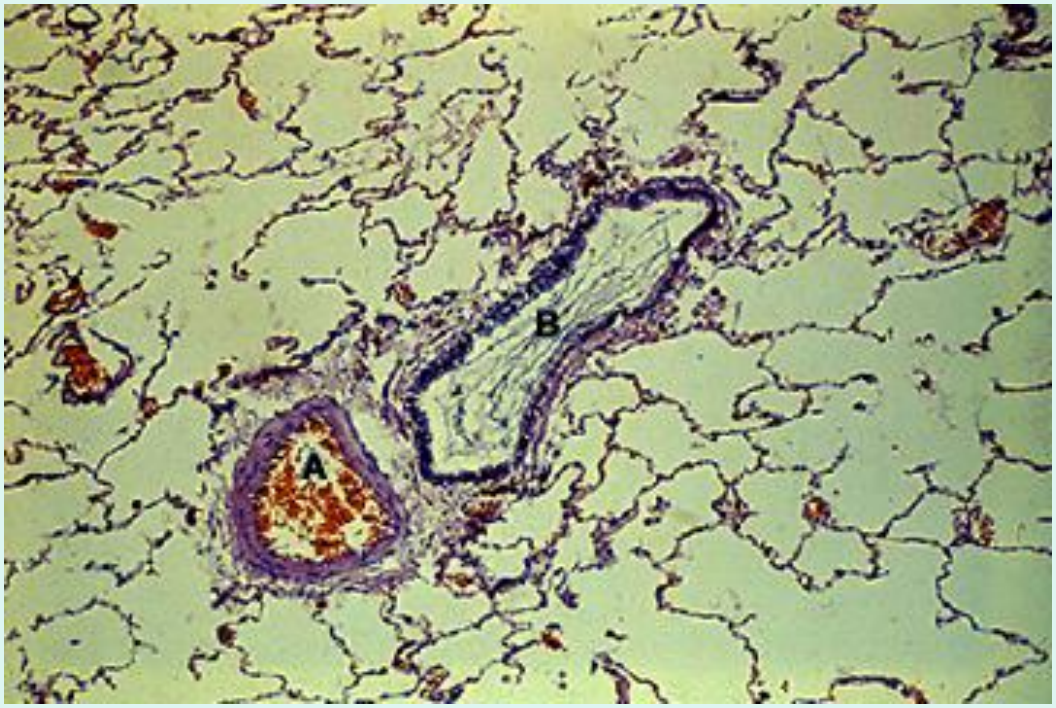
Idiopathic Pulmonary Fibrosis

- Age of onset 50-70, slight male predominance
- Increasing Incidence
- Insidious onset of DOE and nonproductive cough
- Family History (Familial Pulmonary Fibrosis)
- PE shows bibasilar late inspiratory dry crackles or velcro crackles
- Serologies to r/o CTD
- CXR/HRCT
- Pathology: UIP pattern, not necessary if classic hx and radiographic pattern

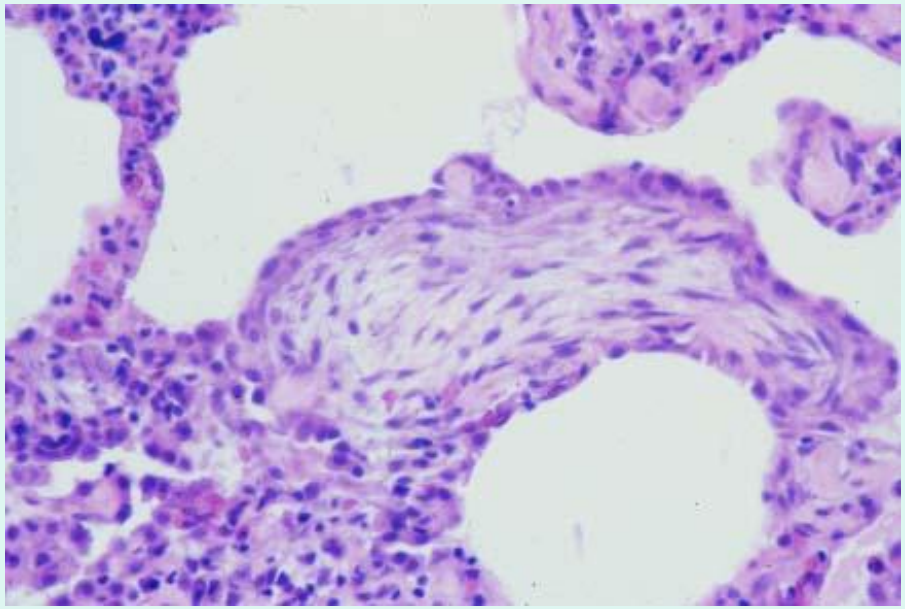
Imaging

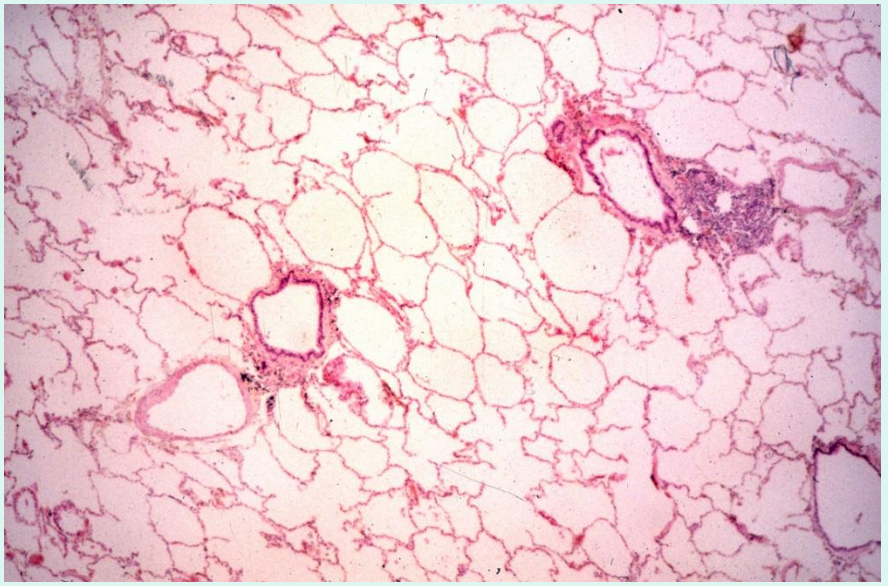


Normal Lung



Pathology





Pathogenesis

- Genetic Predisposition + Inciting Event + Uncontrolled/Abnormal Repair Mechanism (Inflammatory, Immune, Fibrosis)
- Genetic Predisposition
- Initiation Event
  - Smoking
  - Inhalational Injury
  - Virus
- Inflammation

Treatment

?

Treatment

- No therapy has been proven to be efficacious
- Supportive care (O2, pulm rehab, vaccines)
- Consider referring to clinical trials
- Immunosuppressant/Antioxidant Therapy
  - Prednisone + azathioprine + NAC (PANTHER trial)
- Antifibrotic Therapy
  - Pirfenidone
    - Decrease in number of exacerbations; 14% versus 0%
    - Approved in Japan, Canada, Europe

Treatment

- Treat GERD/microaspiration (up to 90% of pts)
- Referral for lung transplantation
- Future Therapies?
  - Thalidomide
  - Tyrosine Kinase Inhibitors
  - Cytokine Inhibitors
  - Growth Factor Inhibitors

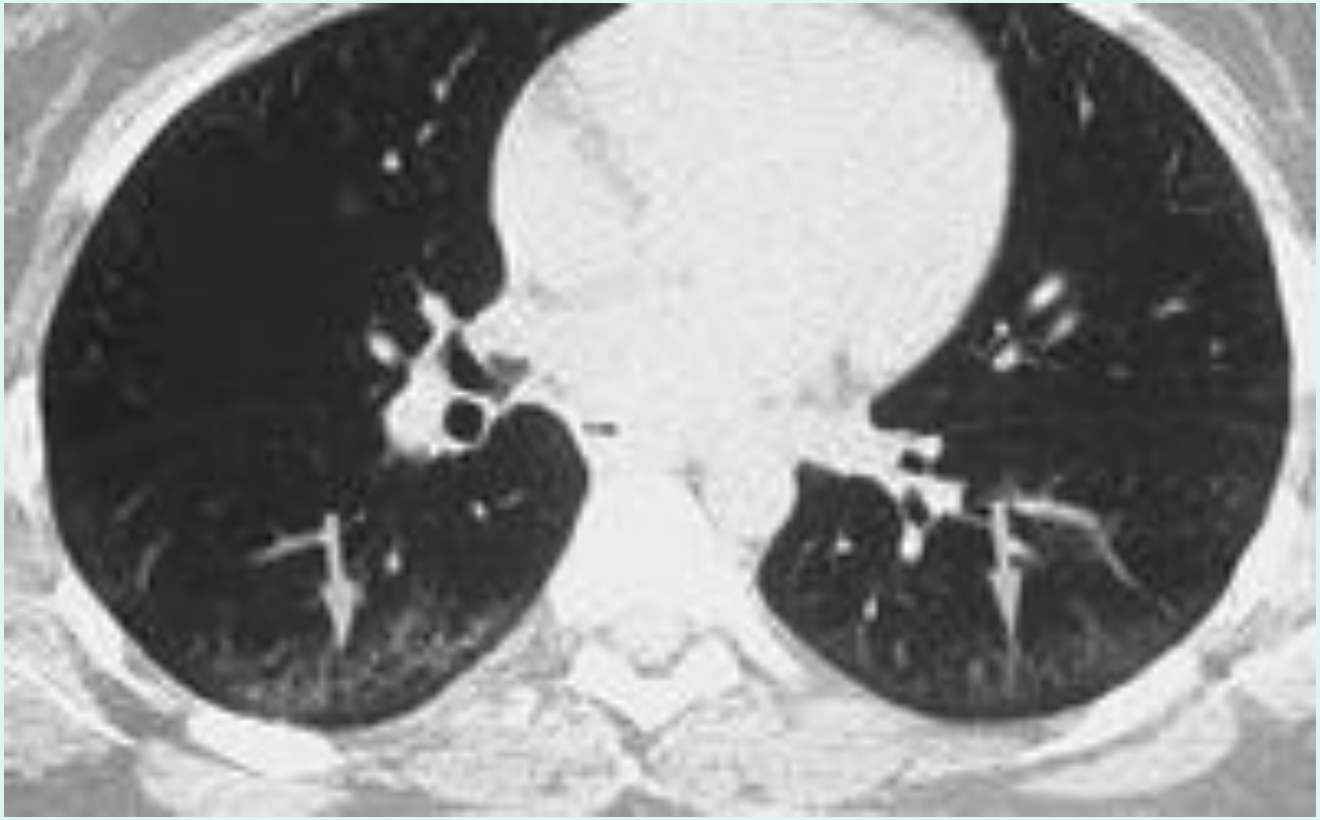
Prognosis/Clinical Course

- Slow, indolent course; mean survival 2-3 yrs since time of diagnosis
- Rapid progression
- Acute exacerbations
  - Rapid, progressive SOB
  - Unknown cause (r/o infection, PE, heart failure)
  - CT will show new GG infiltrates
  - Path shows DAD or acute alveolar injury wirh background of UIP
  - Treatment Solumedrol 1 to 2 gm/day
  - Mortality rate 80%

NSIP

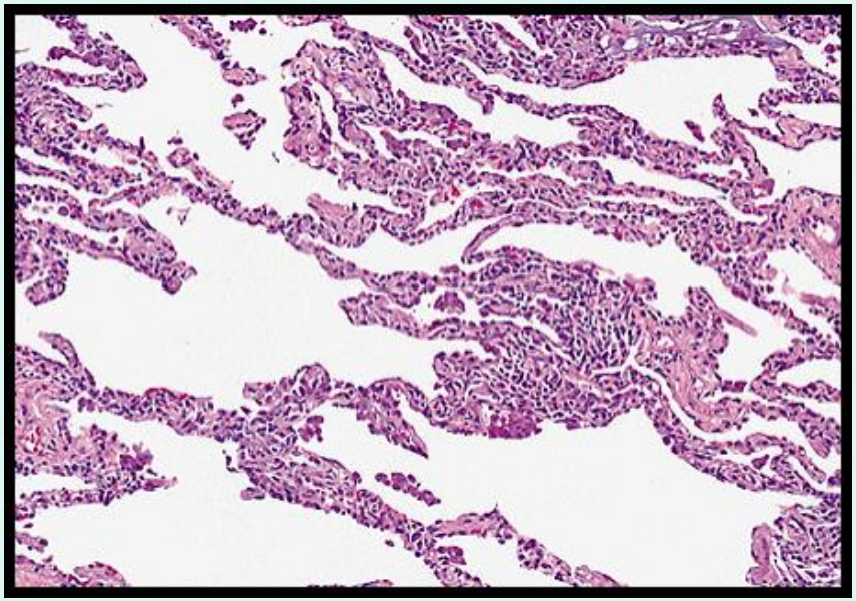
- 40 to 50
- Chronic dyspnea, cough
- PE with bibasilar crackles
- Idiopathic cases but NEED to r/o a known cause (CVD, drugs, HP)
- HRCT shows GG airspace consolidation, and reticular abnormalities
- 2 pathologic patterns: cellular, fibrotic

HRCT

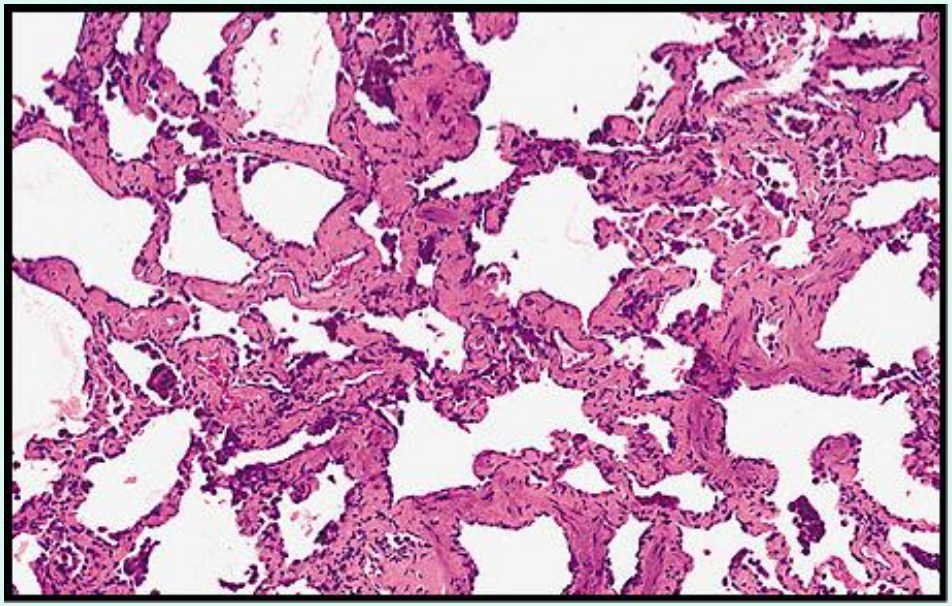


Path

- Cellular NSIP



- Fibrotic NSIP

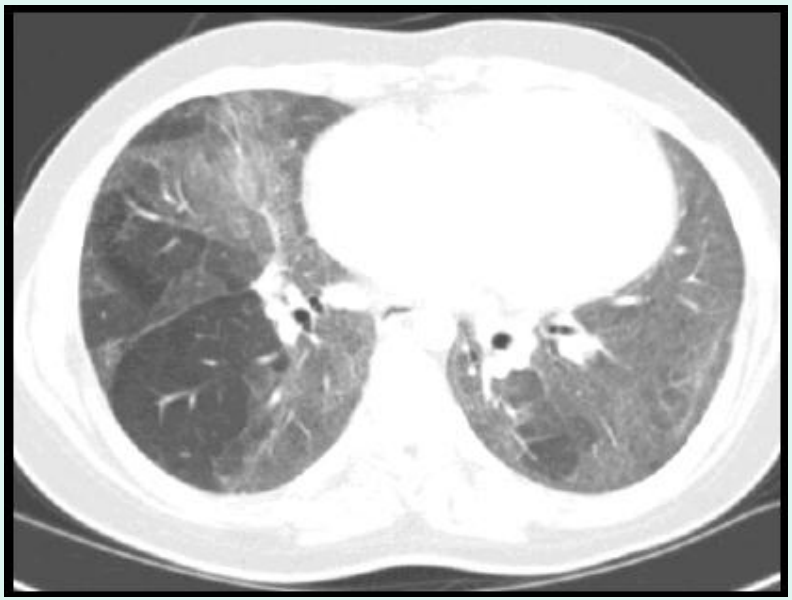


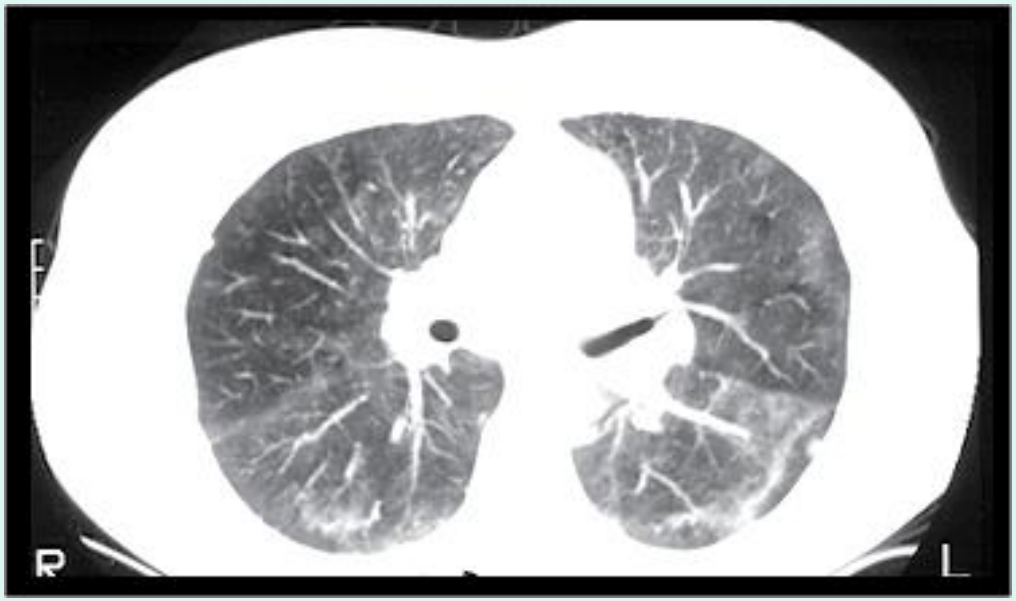
Treatment

- Much better response to treatment
  - Cellular 100%
  - Fibrotic 35-90%
- 5 yr survival; 70%

Respiratory Bronchiolitis-ILD and Desquamative interstitial Pneumonia (RBILD/DIP)

- Young 30-40, CIGARETTE smokers
- Cough, dyspnea. Chronic, progressive sx
- ? Distinct entities vs. a continuum of same disease (RBILD -> DIP)
- HRCT: centrilobular nodules, GG, air trapping
- Path: pigmented laden macrophages in resp. bronchioles (RBILD) and diffusely throughout alveoli (DIP)




R
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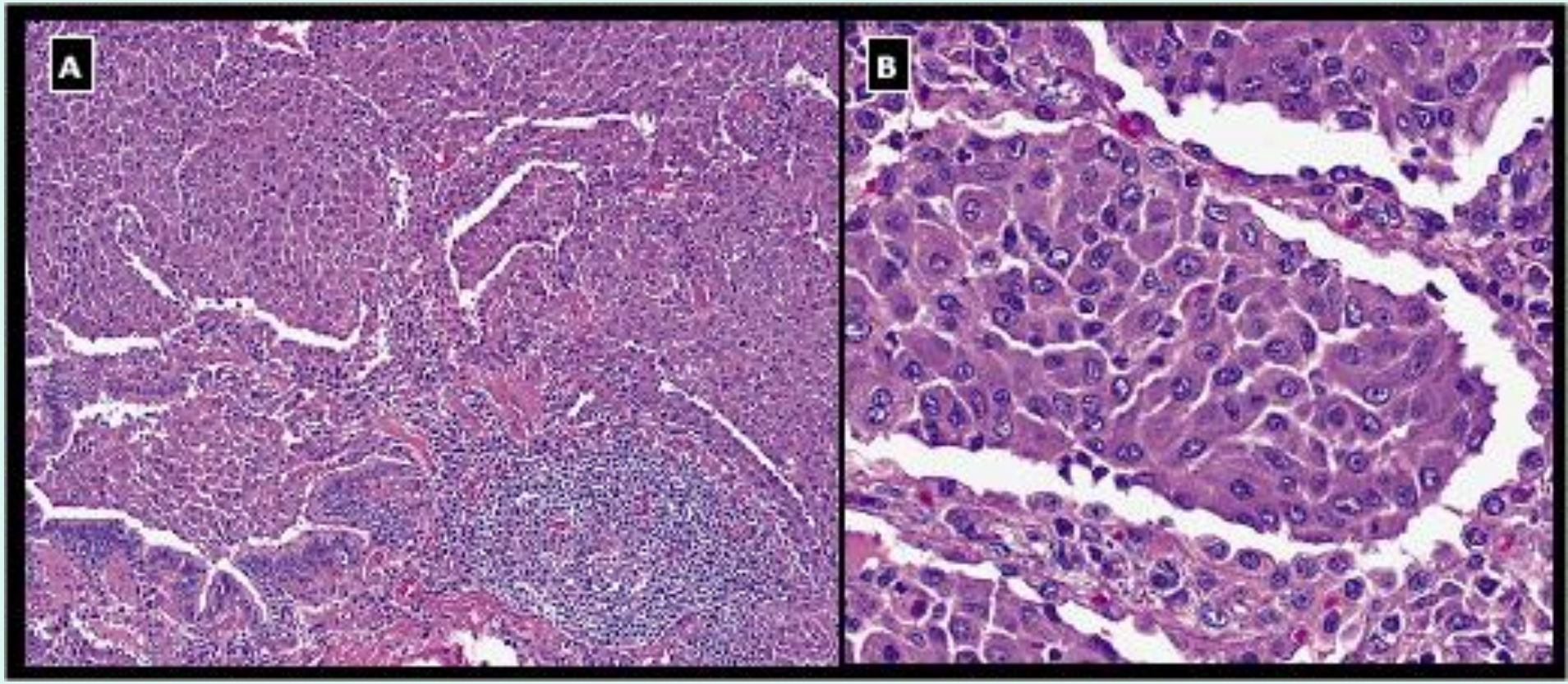
Pathology



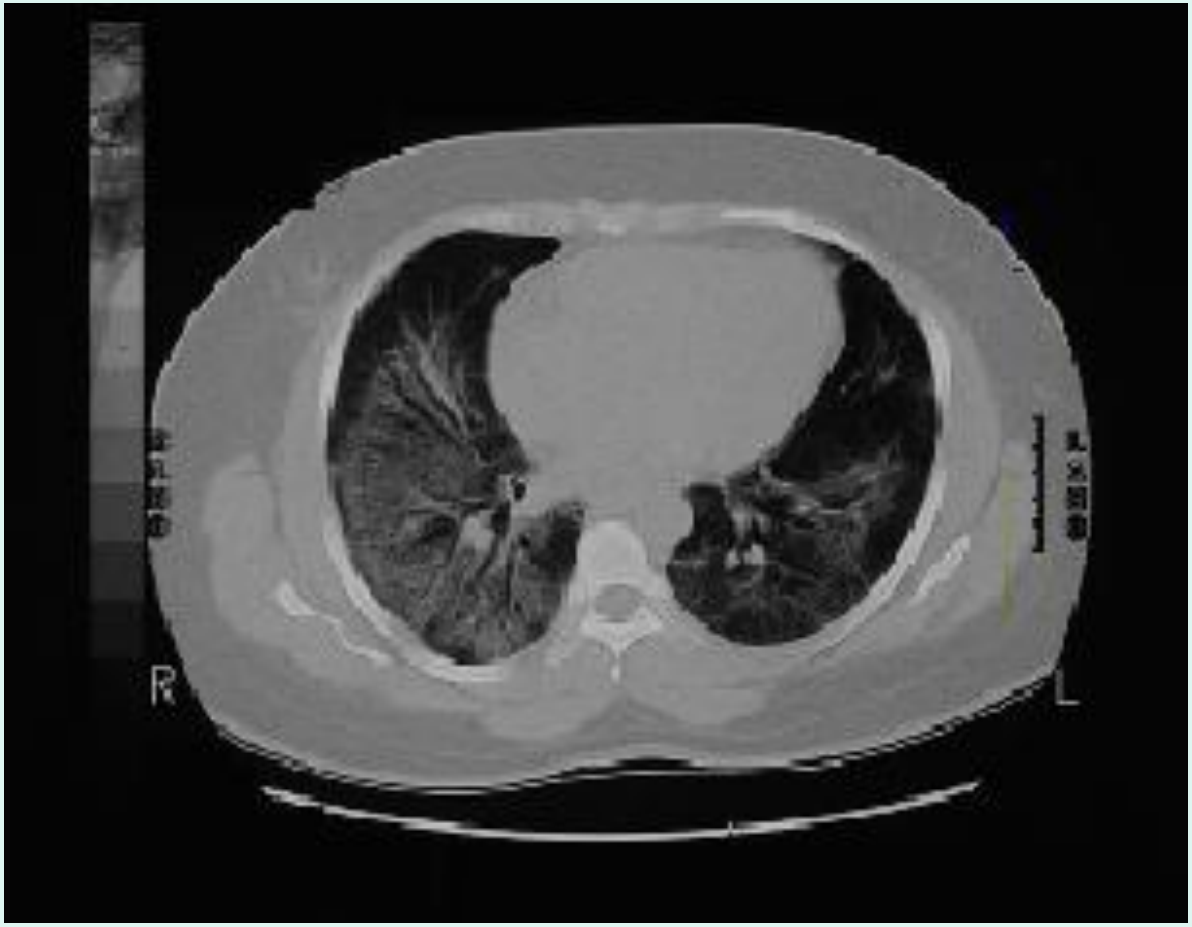
RBILD/DIP

- Treatment: STOP smoking + glucocorticosteroids
- 60% of pts improve
- 5 yr survival of 70%

Acute Interstitial Pneumonia

- Formerly, Hamman-Rich Disease
- Acute to subacute onset of dyspnea and cough, rapidly progressive to resp failure
- Fever
- PE with diffuse insp crackles
- ARDS without a cause
- HRCT with GG infiltrates, consolidation
- Pathology shows DAD

CT



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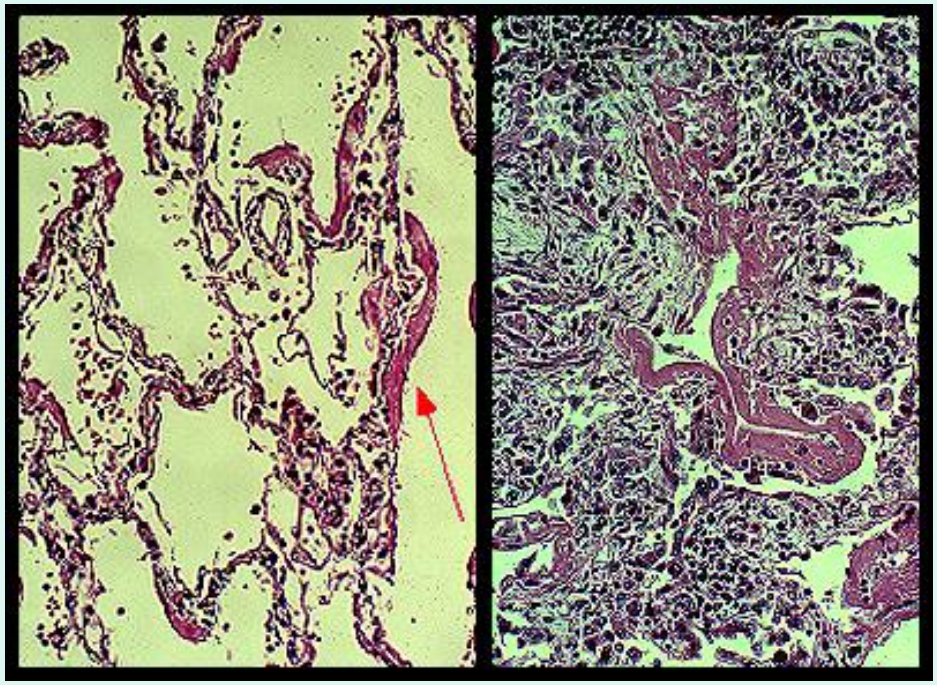
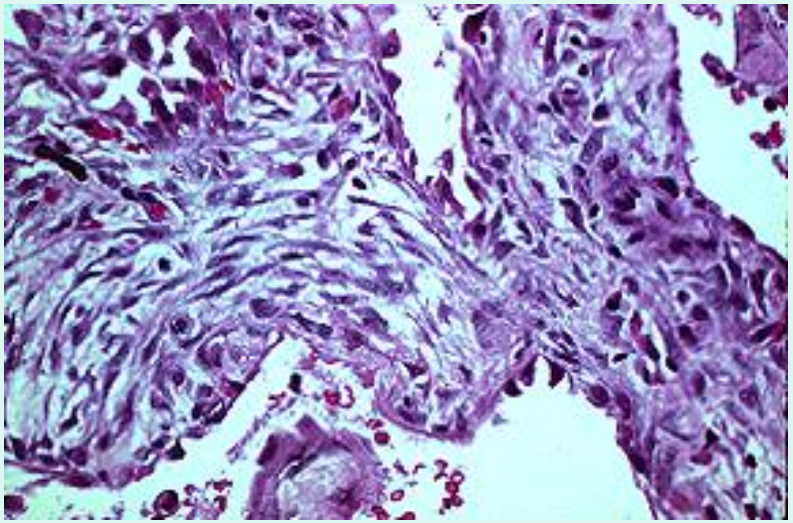




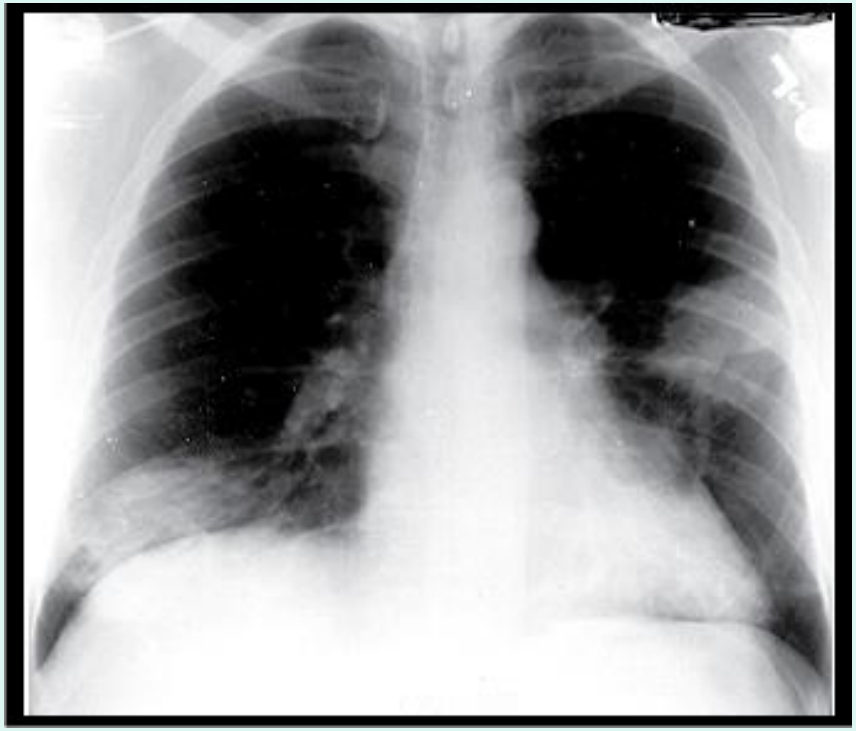
Treatment/Prognosis

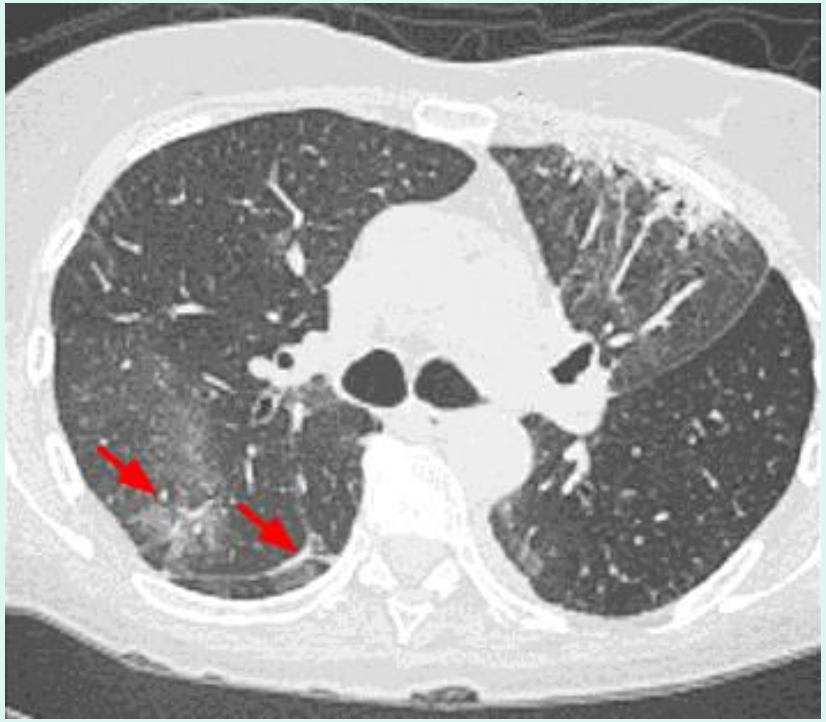
- No proven treatment
  - Most tx with abx, steroids
- Worse survival than ARDS, >50% mortality

COP

- Idiopathic BOOP
- Non-idiopathic causes (post-infectious, drugs, CVD, post-transplant)
- Dyspnea and cough over days to months
- Fever
- Often misdiagnosed as pneumonia
- PE bibasilar crackles
- HRCT with bilateral patchy consolidation, peribronchovascualr nodules

Imaging





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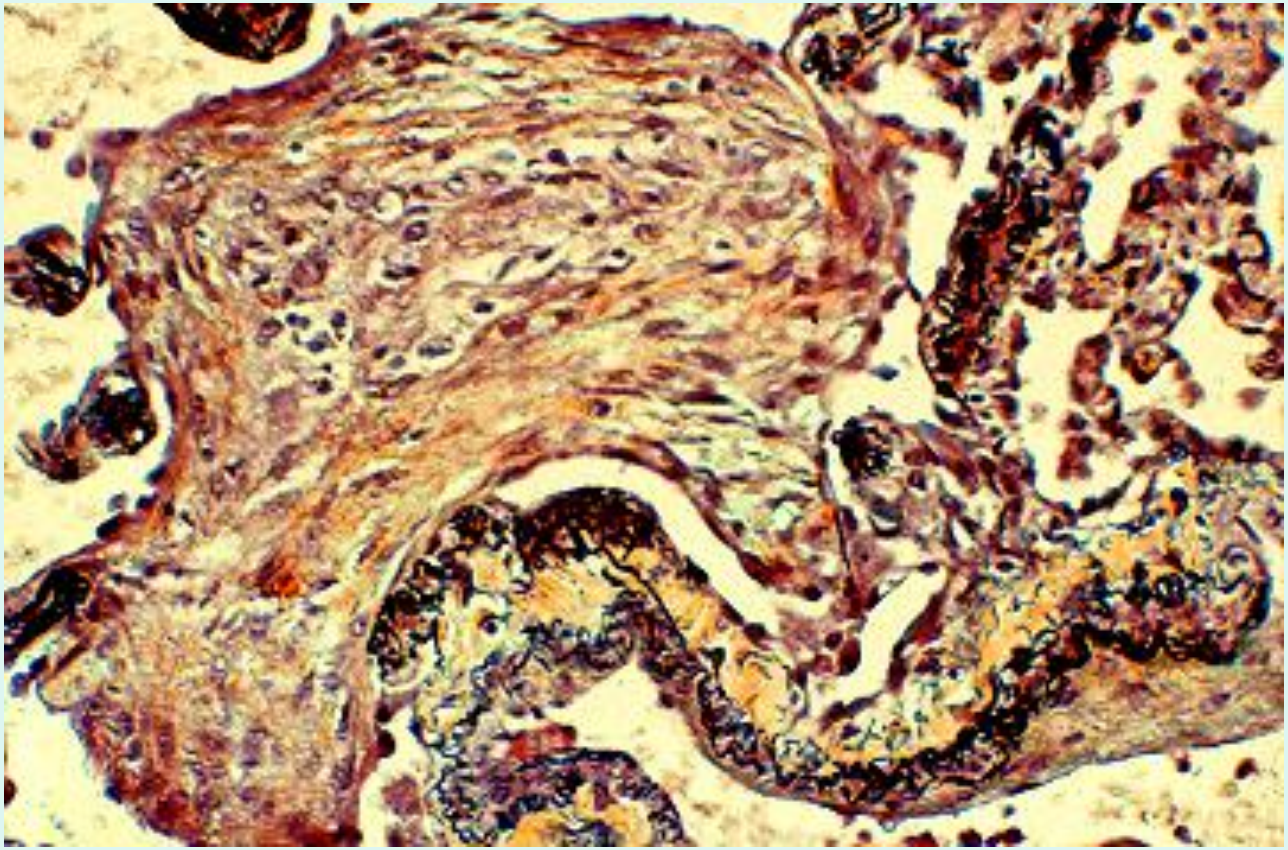


Treatment

- Very responsive to tx with steroids
  - >80% of pts respond to tx
- 5 yr survival close to 100%

Collagen Vascular Disease

- RA
- Lupus
- Systemic sclerosis
- Polymyositis/Dermatomyositis
- MCTD
- Sjogren's
- Relapsing polychondritis
- Ankylosing Spondylitis
- Behcet's Disease
- Systemic vasculitides

- Lung disease
  - Underlying Disease
  - Complication of treatment
  - Opportunistic Infection
- Associated with Increased morbidity and mortality
- Pulmonary Involvement CAN BE initial manifestation of CVD

Rheumatoid Arthritis

- ILD (men > women)
  - Pulm fibrosis
  - BOOP
  - Apical fibrobullous disease
  - Amyloid
- Pleural Disease
  - Effusions
  - Pleuritis
- Rheumatoid Nodules
- Airways Disease
  - Cricoarytenoid arthritis
  - Airflow limitation
  - Follicular bronchitis
  - bO
  - Bronchiectasis
- Drug-Induced
  - MTX
  - Penicillamine
  - Gold
- Pulmonary HTN

Lupus

- ILD
  - Lupus pneumonitis
  - BOOP
  - DAH
- Airways Disease
  - Bronchiectasis
  - BO
  - BOOP
  - Epiglottitis, laryngitis, cricoarytenoid arthritis
- Pleural Disease
- Pulm HTN
- Diaphragmatic Dysfunction/Shrinking Lung Syndrome

Systemic sclerosis

- ILD (25-45%)
  - Pulm fibrosis
  - Aspiration pneumonitis
  - DAH
  - DAD
- Airways Disease
  - Airflow limitation
  - Follicular bronchiolitis
- Pleural Disease
  - Pleuritis
  - Pleural Effusion
  - Spont PTX
- Pulm HTN

Polymyositis/Dermatomyositis

- ILD
  - Pulm fibrosis
  - Aspiration pneumonitis
  - BOOP
  - DAH
  - DAAD
- Aspiration Pneumonia
- Respiratory Muscle Dysfunction
  - Diaphragmatic Dysfxn
  - Atelectasis
  - Vent failure
- Pulm HTN
- Malignancy

Work-up

- RF (anti-CCP)
- ANA
- Scl-70
- CPK, aldolase
- SS-A, SS-B
- Anti-jo 1

Treatment

- DMARDs (Azathioprine, Cellcept, Cyclophoasphamide)
- Pulmonary involvement associated with reduced survival
- Prognosis is better then “idiopathic” cases

Drug-Induced

- Amiodarone
- Bleomycin
- Busulfan
- Chlorambucil
- Carmustine
- Flecainide
- Gold
- Methotrexate
- Nitrofurantoin
- Taxol/taxotere

Occupational

- Asbestosis
  - Plumbers, Pipefittersm Electricians, Insulation Workers, Construction, Shipbuilders, Railways
- Silicosis
  - Miners, masonry, Sandblasting, Foundry, Ceramics, Glass Maufacturing
- Berylliosis
  - Machine shops, electronics, defense industry

Hypersensitivity Pneumonitis

- Immunolgic reaction to an inhaled agent (organic)
- Cigarette smoking associated with decreased risk of HP

Occupations

- Farming, vegetable, or dairy cattle workers
- Ventilation and water-related contamination
- Bird and poultry handling
- Veterinary work and animal handling
- Grain and flour processing
- Lumber milling, construction, wood stripping, paper manufacturing
- Plastic manufacture, painting, other chemicals
- Textile workers

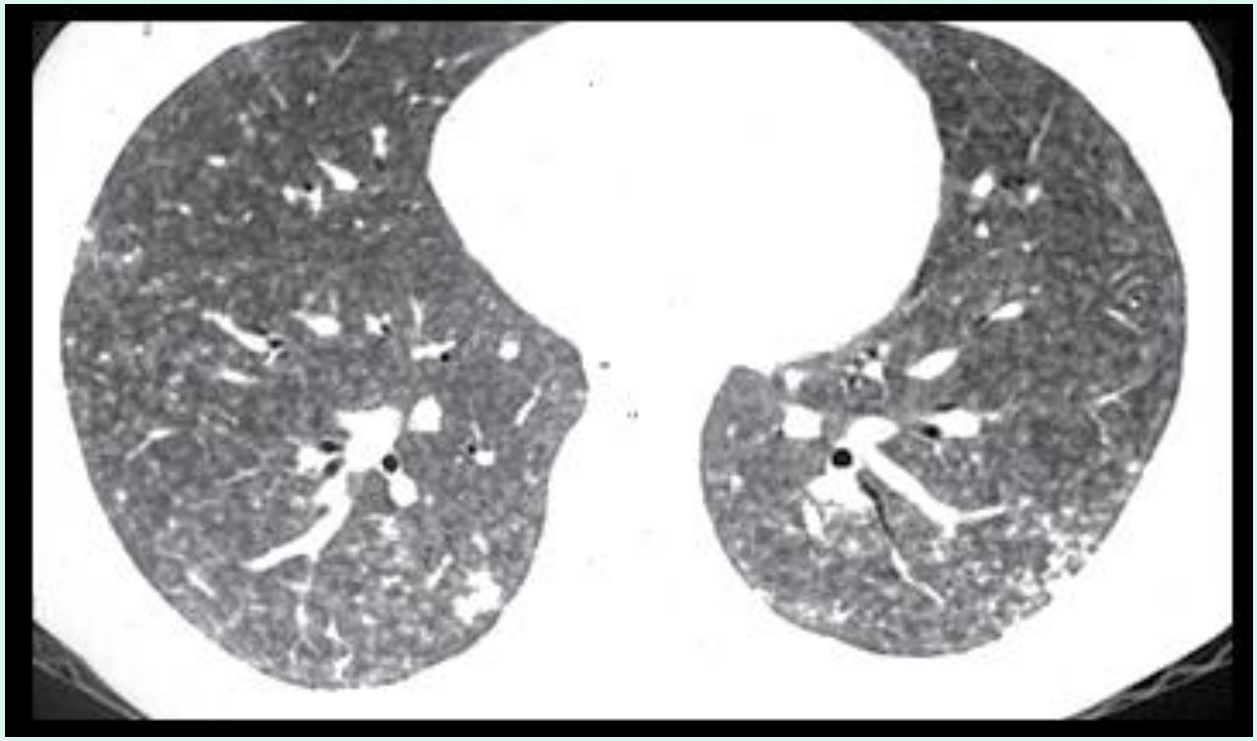
Acute HP

- 4 to 6 hrs following an acute exposure
- Fevers, chills, malaise, cough, dyspnea, wheezing
- May be confused with an infection
- Removal of exposure results in resolution of sx, usually days
- CXR – micronodular interstitial pattern in mid-lower lung zones
- Path – poorly formed noncaseating granulomas

Subacute HP

- Fatigue, anorexia, weight loss, productive cough, dyspnea
- CT shows nodules, GG, mild fibrotic changes in upper lungs
- Treatment removal from exposure and glucosteroids

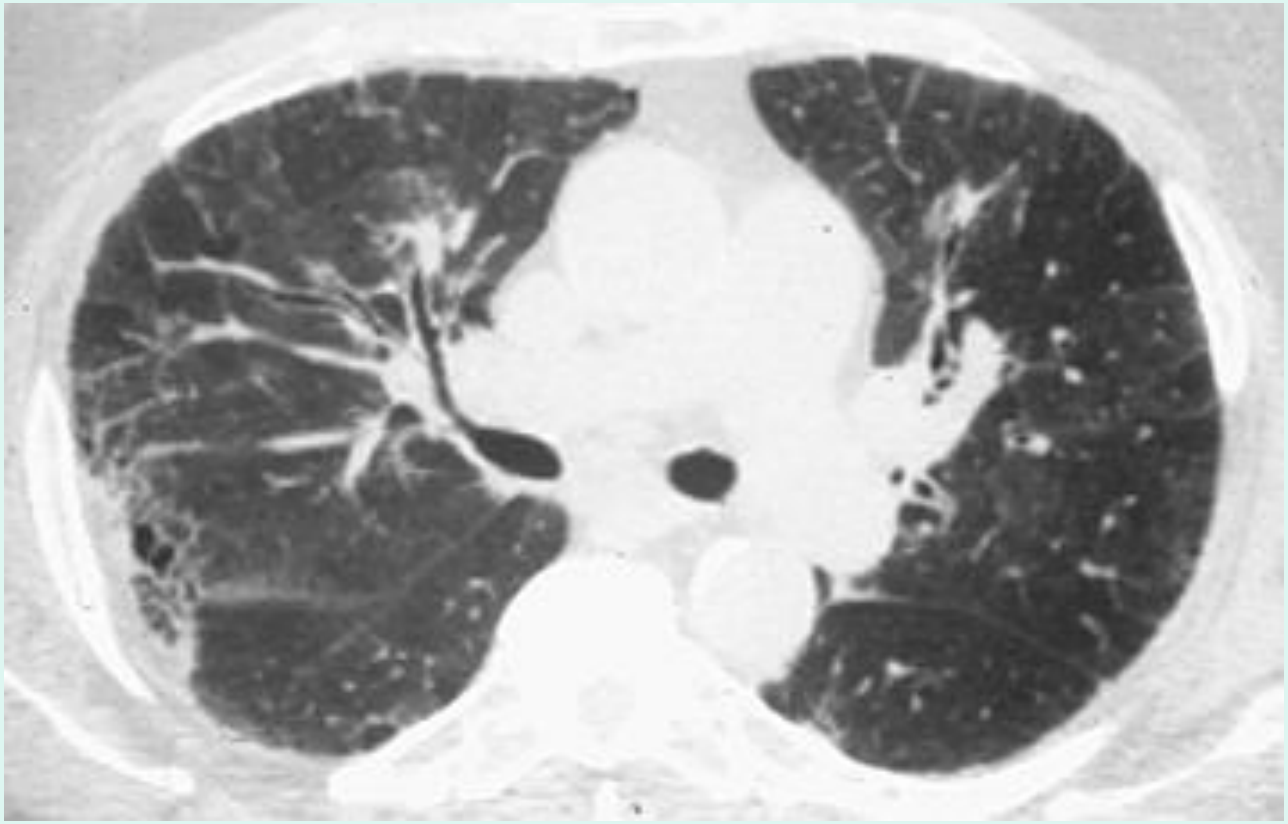
HRCT



Chronic HP

- Insidious onset of cough, DOE, fatigue, weight loss
- HRCT with GG, micronodules accompanied by honeycombing
- Often misdiagnosed as IPF

HRCT



Sarcoidosis

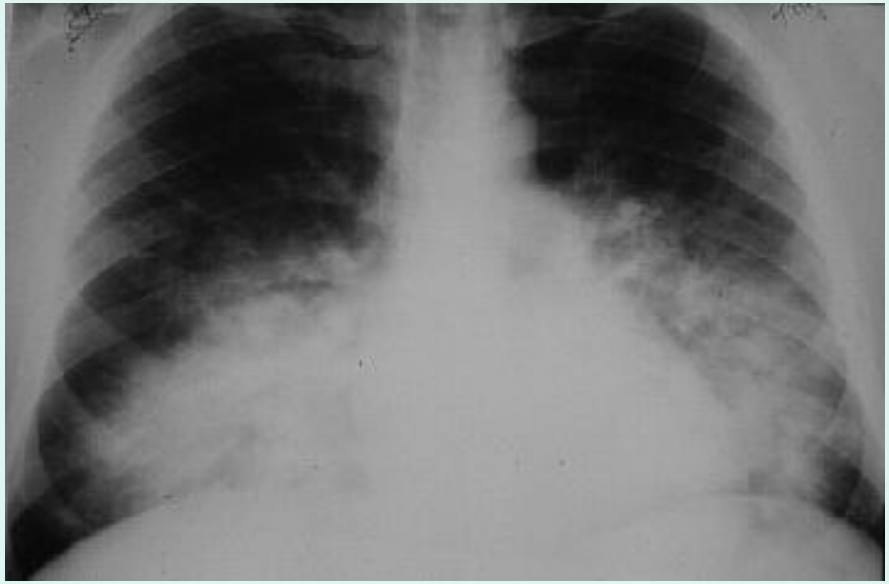
- Radiographic Stages
  - O : No disease
  - I : B hilar/mediastinal LAD
  - II : LAD + diffuse interstitial pattern
  - III : parenchymal disease w/o nodal enlargement
  - IV : pulm fibrosis with honeycomb changes
- Bronchoscopy
  - Increased CD4/CD8 ratio
  - TBBx yield 40-90%
  - Noncaseating granulomas
- Prognosis
  - 2/3 spont remission
- Treatment
  - Pred + MTX
  - Azathioprine, hydroxychloroquine, CPA

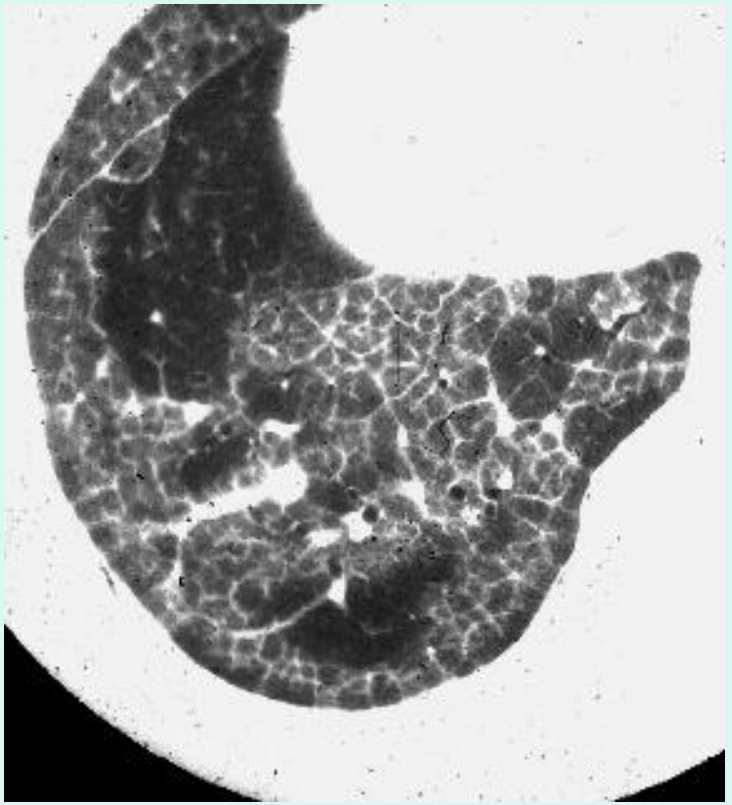
Pulmonary Alveolar Proteinosis

- 30 to 50
- 2:1 male predominance
- Dyspnea
- 1/3 of pts asx and present with “abnl CXR”
- Caused by decreased GM-CSF protein or altered fxn. Large % of adults will have autoantibodies.

- CXR with B alveolar opacities in “bat-wing”
- HRCT with GG opacities, thickened intralobular septa in polygonal shapes “crazy-paving”
- Bronch is usually sufficient to make dx
- Filling of alveolar spaces with PAS + lipoproteinaceous material
- Tx
  - **Whole lung lavage (20L)**
  - **GM-CSF**

Chest imaging





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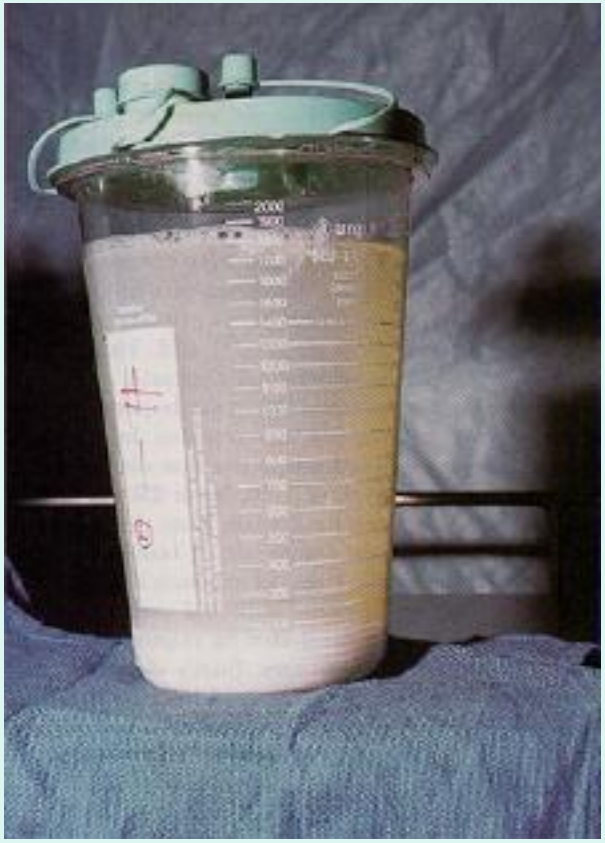
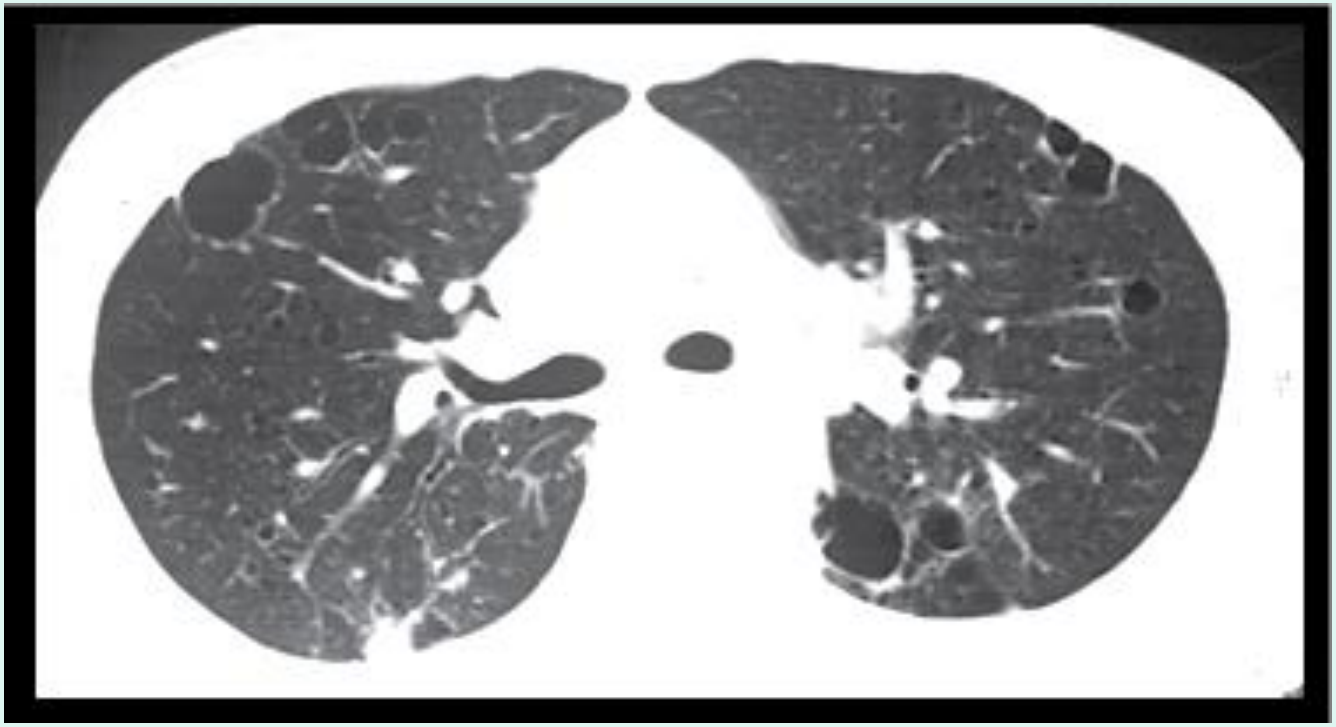


Pulmonary Langerhans' Cell Histiocytosis

- Isolated lung involvement (85%)
- Multisystem Syndrome (lungs, bone, skin, pituitary, liver, LN, thyroid)
- 20 to 40
- CIGARETTE smokers (90% current smokers)
- Nonproductive cough, dyspnea, pleuritic CP
- 1/3 constitutional symptoms
- PTX 15-25%
- Extrapulmonary sx (bone pain, DI, rash, LAD)

CT



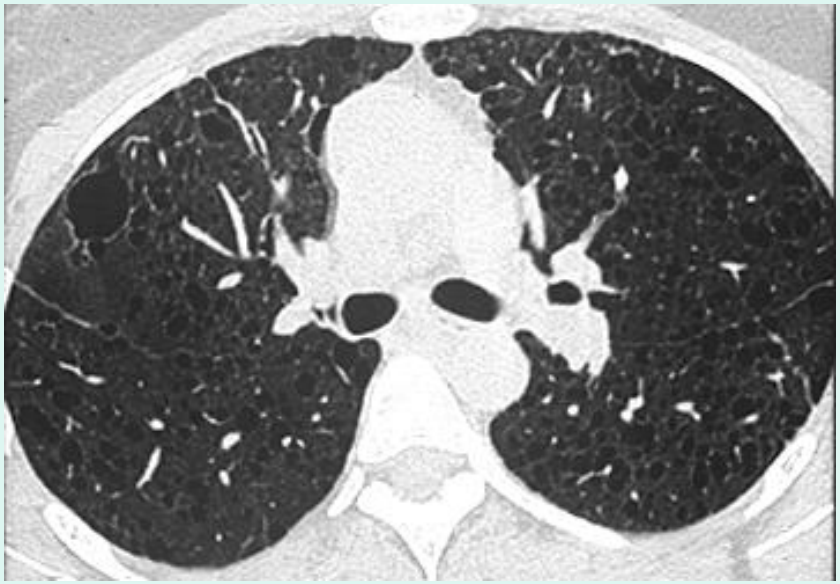
Treatment

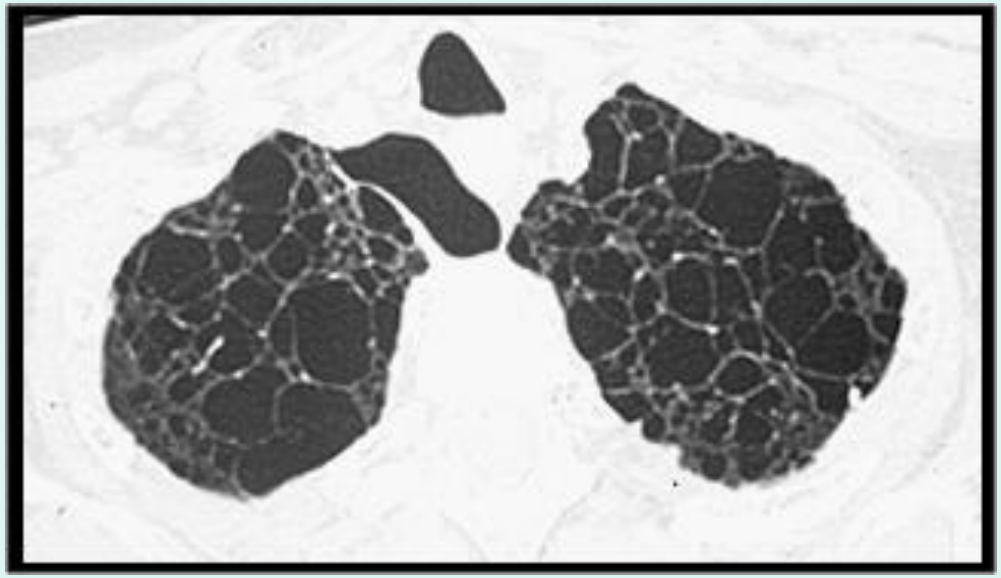
- Smoking cessation
- In most, sx stabilize with quitting alone
- Corticosteroids in those with progressive disease or persistent sx despite quitting
- Prognosis
  - 50% respond to no tx other then smoking cessation
  - 10-20% rapid progression -> fibrotic lung disease
- 5 yr survival 74%
- Referral for lung transplant (recurrence may occur)

Lymphangioleiomyomatosis (LAM)

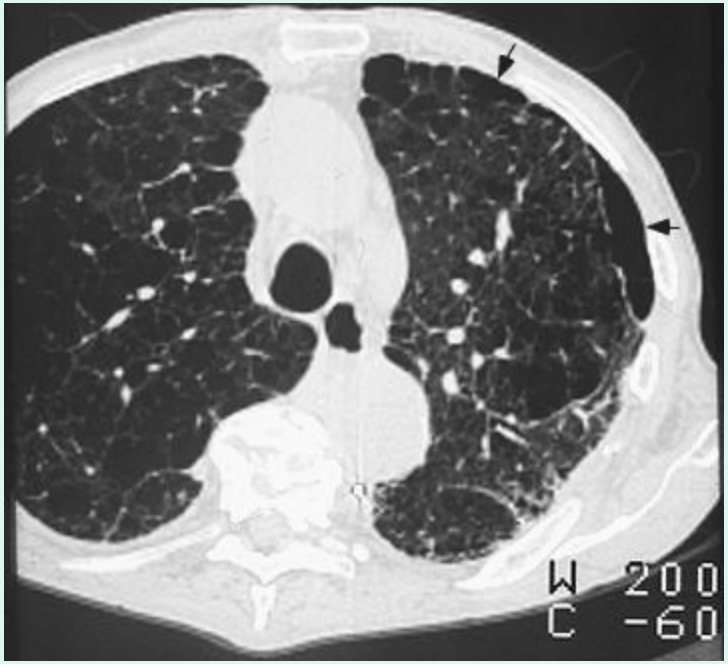
- Almost exclusively premenopausal women
- Dyspnea, cough, CP, PTX
- 50% initial presentation PTX (81% during course of disease)
- Chylous effusions, ascites
- 50% renal angiomyolipomas
- Associated with TSC-2
- Proliferation of atypical SM cells around airways blood vessels, lymphatics

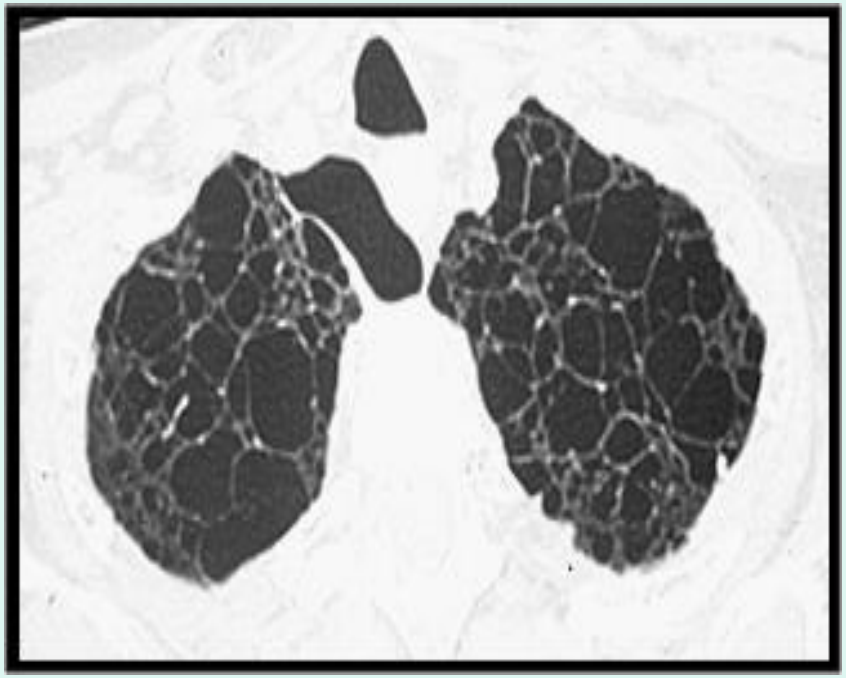
CT



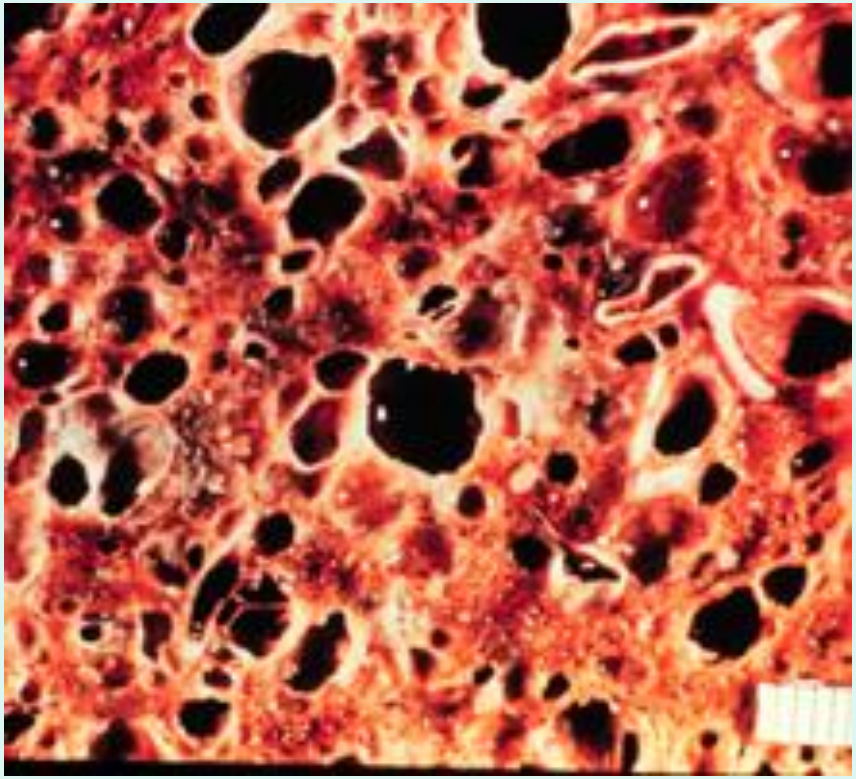


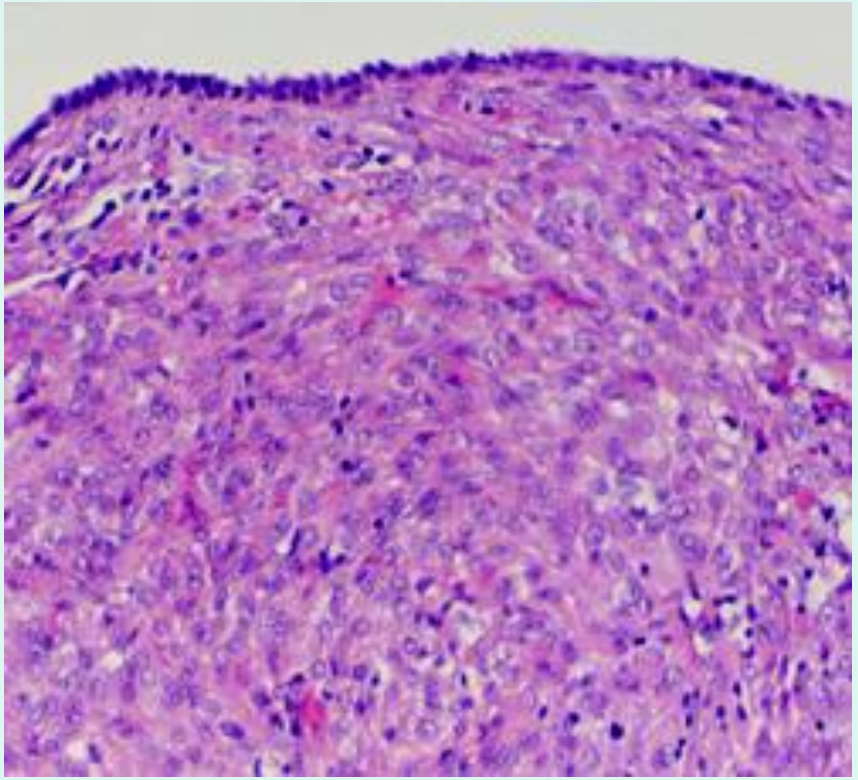
Bleb vs. Cyst





Pathology





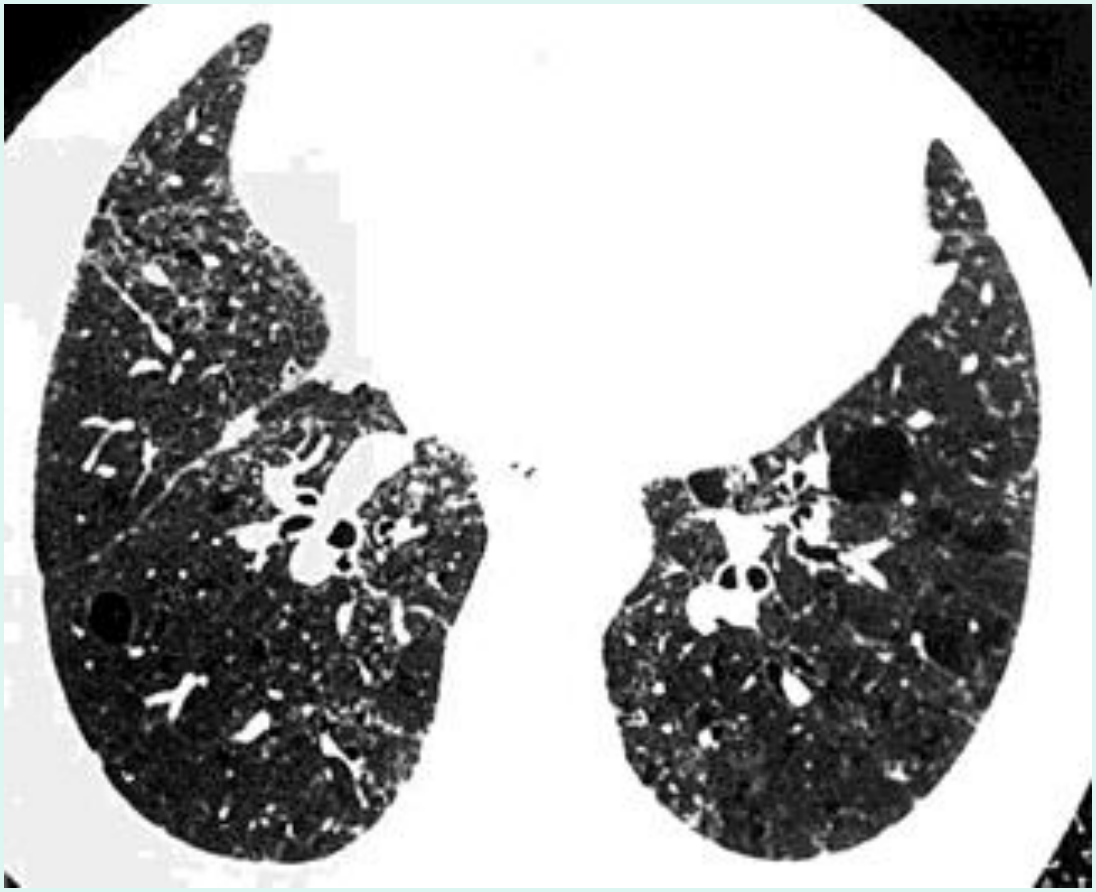
Treatment

- Pregnancy and supplemental estrogen may accelerate disease
- Hormonal manipulation
  - Oophrectomy
  - Progestin
  - Tamoxifen
  - LH-RH
- Most will have progressive decline and will need to be referred for transplant (may recur in allograft)
- Median survival 8-10 yrs

LIP

- Idiopathic, RA, Sjogren's, HIV, Congenital Immunodeficiency
- 30 to 50, predominantly female
- Constitutional sx
- Slowly progressive DOE
- Bibasilar crackles, LAD
- CT with GG infiltrates, centrilobular nodules, LAD, cysts
- Path: Dense interstitial infiltrates of lymphocytes, plasma cells, and other lymphoreticular elements

CT



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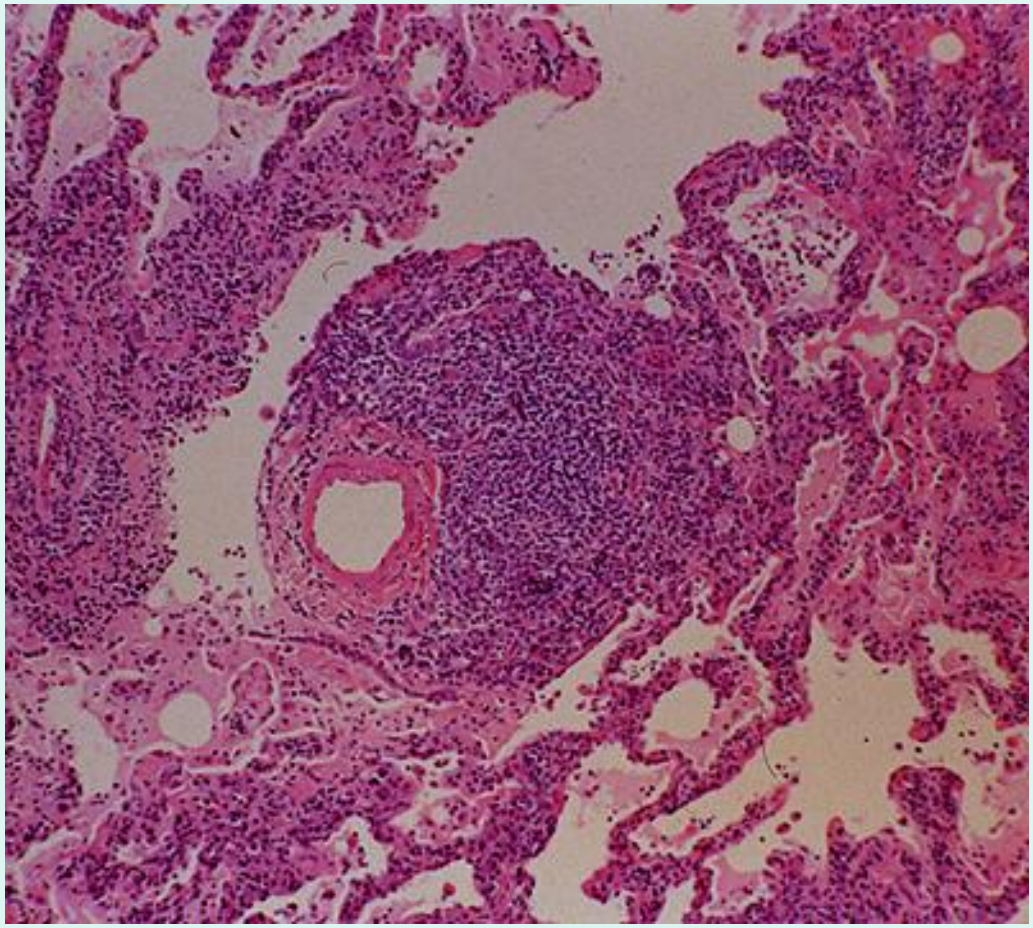

Treatment

- Corticosteroids +/- immunomodulation therapy
- Most stabilize or improve (60%)
- 40% rapid decline
- 5 yr mortality 60%
- ? Possible malignant transformation to lymphoma

Summary

- Take a HISTORY
- Identify an underlying condition, may effect treatment and prognosis
- Fibrosis = BAD

Case #1

- 66 yo female with dry cough and DOE @ 1 block (had been attributed to aging, weight gain) for up to 2 yrs
- On ROS: intermittent heartburn, myalgias, joint pain in wrists and elbows, ?Raynaud's phenomenon
- Social Hx unremarkable
- Family Hx + mother with pulm fibrosis (no bx performed)

- PE remarkable for bibasilar crackles, periungal erythema, slt thickened skin on her fingers
- PFTs:
  - FEV1 2.04 (81%), FVC 2.45 (78%), ratio 83%, DLCO 65% with DLCO/VA 110%
- HRCT: Subpleural interstitial thickening with mild contraction bronchiectasis

- Serologies sent:
  - ANA 1:160 homogeneous
  - Scl-70, RF, anti-CCP, dsDNA, SSA, SSB, CPK, Aldolase negative
- ECHO showed mild pulm htn

Diagnosis

- Scleroderma