Interstitial Lung Disease

Nitin Bhatt, MD
Assistant Professor of Internal Medicine
Division of Pulmonary, Allergy, Critical Care, and Sleep Medicine
Ohio State University Medical Center

Case #1

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Jim Allen, MD
Professor of Internal Medicine
Division of Pulmonary & Critical Care Medicine
Ohio State University Medical Center

Case #1

- **57 y.o. WM with a history of shortness of breath and cough that has been present for 1 year**
- **Initially worse with walking, moderate exertion. No resting symptoms.**
- **Now activity limiting**
- **Associated with a dry, nonproductive cough**
- **Negative cardiac evaluation**

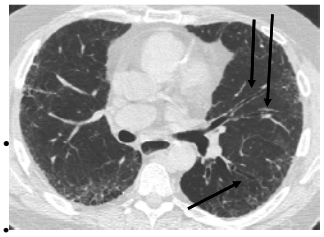
- **PMHx: HTN**
- **Meds: HCTZ**
- **SOCHx: 30 pack year smoking history, quit 10 years ago**

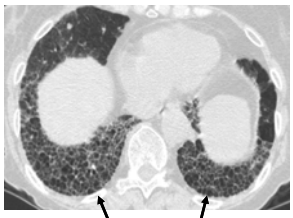
Case #1

- PE: HR 78, BP 138/67, sats 96% on room air
  - Lungs with bibasilar dry crackles
  - Ext with clubbing
- PFTs:
  - FVC 69% predicted
  - FEV1 72%
  - TLC 62%
  - DLCO 53%
  - 6 Minute walk: Walks 1100 feet with an initial sat of 96% dropping to 79% on room air

Case #1

- CT scan
  - Traction bronchiectasis

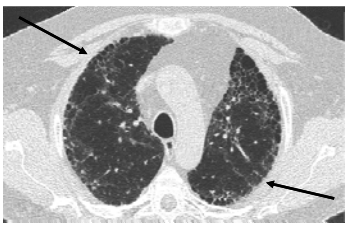




Honeycombing

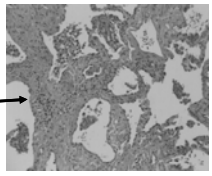
Case #1

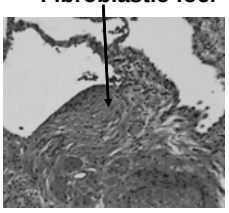
- CT scan
  - Subpleural fibrosis

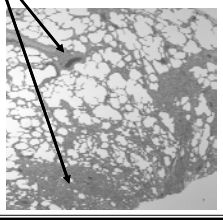


Case #1

- Lung biopsy
  - Interstitial thickening
  - Temporal heterogeneity
  - Fibroblastic foci







Idiopathic Pulmonary Fibrosis

- Most common ILD of unknown etiology
- Mainly affects people > 50 yo, most are over the age of 60 yo
- Incidence is estimated at 7.4-10.7 cases per 100,000 per year
- Prevalence of IPF is estimated at 13-20/100,000
- Most are current or former smokers
- Potential risk factors for developing IPF include cigarette smoking, occupational/environmental exposures

Idiopathic Pulmonary Fibrosis

- Diagnosis based on imaging, lung biopsy
- High resolution chest CT scan can be very specific for the diagnosis of IPF
  - Subpleural, basal predominance
  - Interstitial/reticular infiltrates
  - Honeycombing with or without traction bronchiectasis
- Biopsy findings: Usual interstitial pneumonitis (UIP) pathologic pattern
  - Temporal heterogeneity
    - » Alternating areas of normal lung, interstitial inflammation, fibrosis, and honeycombing
  - Most severe in the subpleural region of the lung
  - Fibroblastic foci

Idiopathic Pulmonary Fibrosis

- History/Exam
  - Gradual onset and progressive dyspnea and/or a nonproductive cough
  - Bibasilar inspiratory crackles (Velcro crackles)
  - Clubbing also common
  - Later in the clinical course, signs of right heart failure and peripheral edema
- No characteristic lab findings
  - Positive autoimmune serologies
- PFTs show restriction, low diffusing capacity and desaturation with exertion

Idiopathic Pulmonary Fibrosis

- Prognosis
  - Progressive course, acute exacerbations
  - 80% mortality at 5 years
- Treatment
  - No evidence of benefit in patients with IPF treated with corticosteroids alone or a combination corticosteroid and immunosuppression
  - Participation in clinical trials encouraged
  - Supplemental oxygen
  - Pulmonary rehabilitation
  - Treatment of GERD
  - Lung transplant evaluation

Case #2

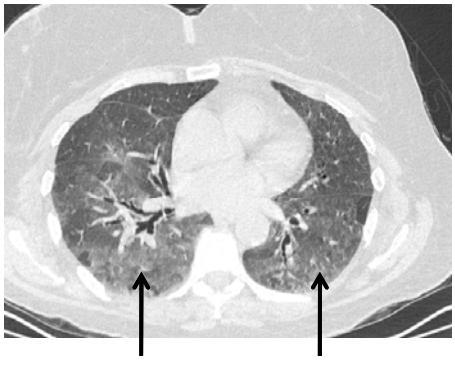
Pulmonary Function Tests

• FVC	1.88	50%
• FEV1	1.59	58%
• TLC	3.84	77%
• DLCO	13.1	66%

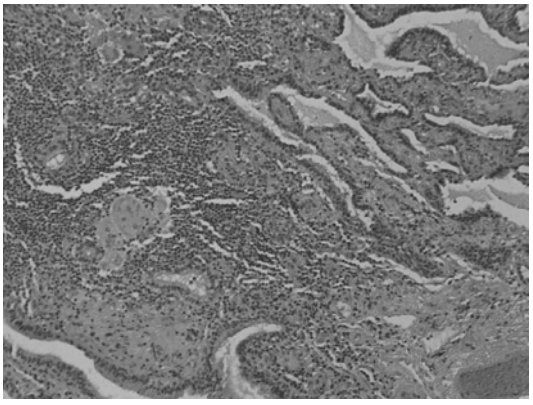
Restriction with a low diffusing capacity

Case #2

- **64-year old woman with 1 year history of cough and dyspnea**
- **Started on home oxygen 6 weeks previously**
- **Past medical history: uterine CA 1998 (hysterectomy & XRT)**
- **Social history: non-smoker with feather pillow**
- **Exam: basilar crackles without digital clubbing**



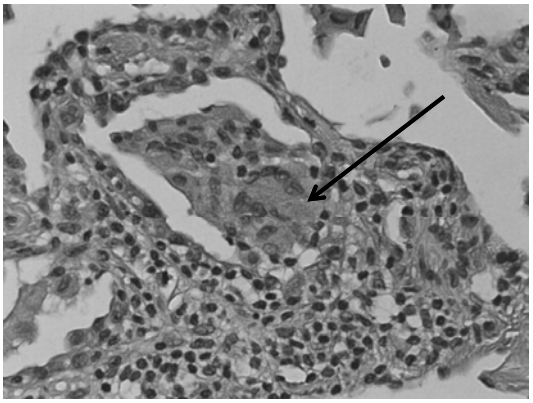
Diffuse Ground Glass Infiltrates



Lymphocytic & granulomatous infiltrates

Hypersensitivity Pneumonitis

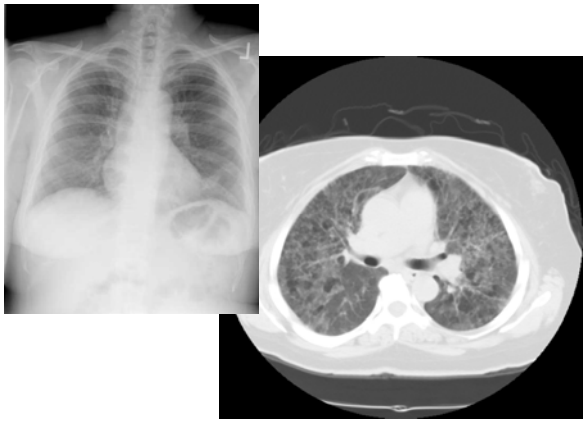
- Etiology often hard to identify
  - Birds, feathers, down
  - Hot tubs
  - Occupation
  - Drugs
- Pathology:
  - T-suppressor cell alveolitis
  - Poorly formed granulomas
- Laboratory:
  - Serology can aid in clinical assessment
- Treatment:
  - Remove offending antigen
  - Prednisone
- Outcome:
  - Complete resolution
  - Chronic fibrosis



Poorly-formed granulomas

Photo: Kathrin Gaisser

Photo: David Shankbone



Case #3

- 49yo AAF with a several month history of progressive cough, SOB/DOE especially climbing stairs
- Rash involving face, neck
- GERD and dysphagia

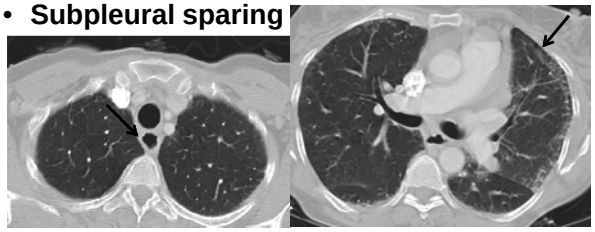
- PMHx: (-)
- SOCHx: non-smoker, no exposures

- Exam: basilar dry crackles, no clubbing, rash, synovitis
- PFTs: restriction, no desat with exertion
- Autoimmune evaluation: (+) ANA, (+) CK

Case #3

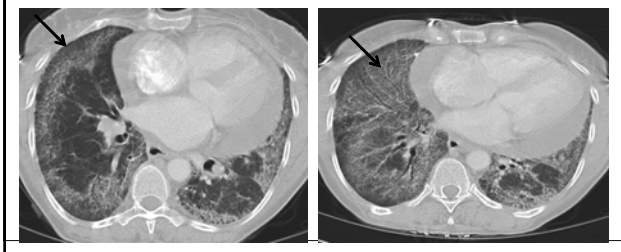
Case #3

- Interstitial infiltrates
- Subpleural sparing



Case #3

- Ground glass infiltrates
- Subpleural sparing of infiltrate and fibrosis
- No honeycombing

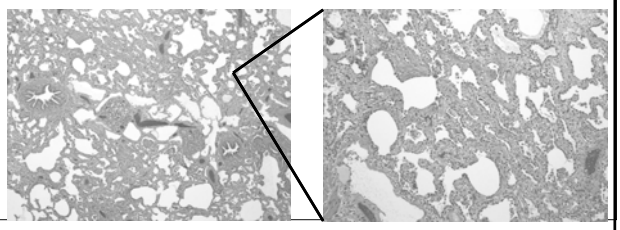


Non-Specific Interstitial Pneumonitis

- Second most common idiopathic interstitial pneumonia
- Affects men and women equally with an average age about 10 years younger than IPF
- Shortness of breath and dry cough
- Physical findings include inspiratory crackles, clubbing
- Often associated with autoimmune disease
  - Patients with connective tissue disease, especially systemic sclerosis and polymyositis/dermatomyositis
  - Lung disease can precede signs of systemic autoimmune disease

Case #3

- Interstitial fibrosis
- Temporal homogeneity



Non-Specific Interstitial Pneumonitis

- High-resolution CT
  - Nonspecific combination of ground glass opacities, consolidation, and irregular lines
  - Peripheral subpleural distribution, lower lung
  - Subpleural sparing
- Pathology
  - Temporally uniform interstitial inflammation with varying degrees of fibrosis
  - Cellular NSIP
    - » Prominent inflammation without significant fibrosis
  - Fibrotic NSIP
    - » Significant fibrosis with little or no inflammation

Non-Specific Interstitial Pneumonitis

- **Important to differentiate from UIP/IPF**
  - **NSIP 5 year mortality <10%**
  - **Survival > 6-10 years**
- **Treatment**
  - **Corticosteroid therapy, generally with corticosteroid and immunosuppressant combination therapy**
  - **Evalaution for underlying autoimmune disease**

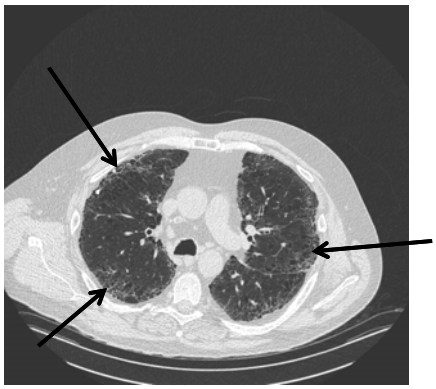
Case #4

- **57 year-old man**
- **Dyspnea for 4 years, now worsening**
- **Started on home oxygen; prednisone course helped but he gained 60 pounds**
- **SH: 42 pack-year smoker; trucker; lives on a farm with a barn and cows**
- **Exam: basilar dry crackles, no clubbing**

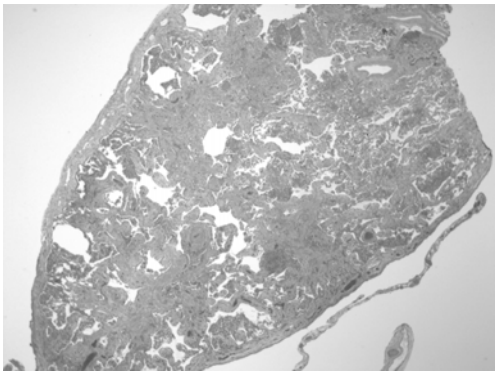
Case #4

Laboratory Testing

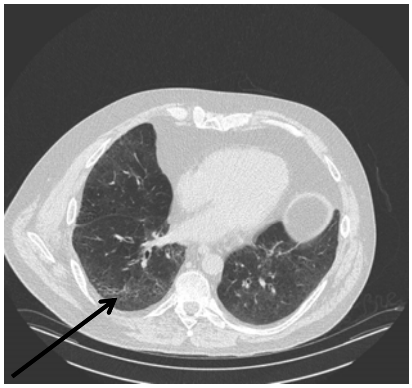
- **Multiplex ANA positive**
  - **Anti-dsDNA positive**
  - **All other autoimmune antibodies negative**
- **Hypersensitivity pneumonitis panel negative**
- **CBC normal**
- **Pulmonary function tests:**
  - **Restriction**
  - **Low diffusing capacity**



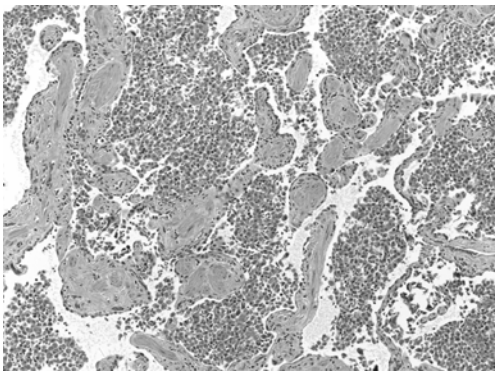
Peripheral reticular infiltrates



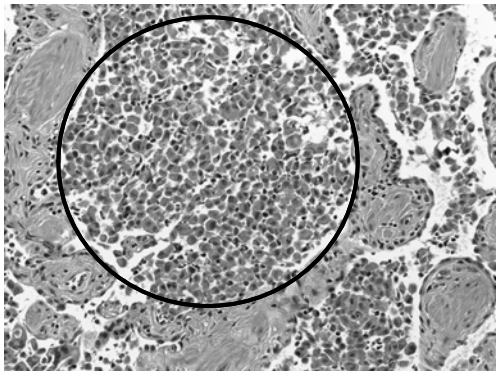
Right Middle Lobe: Low Power



Basilar Ground Glass Infiltrates



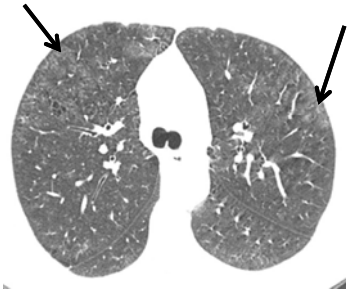
Right Middle Lobe: Medium Power



Right Middle Lobe: High Power

Desquamative Interstitial Pneumonitis Treatment

- Smoking cessation
- Corticosteroids
- Azathioprine
- Cyclophosphamide
- Mycophenolate?



Prognosis is generally good

Desquamative Interstitial Pneumonitis

- > 90% are smokers
  - Rarely associated with collagen vascular disease
- Typical age = 30-50
- Chest CT:
  - Ground glass infiltrates
  - CXR may be normal
- Pathology:
  - Abundant smoker's macrophages
  - Little alveolar wall inflammation
- Frequently overlaps with respiratory bronchiolitis interstitial lung disease

Case #5

Case #5

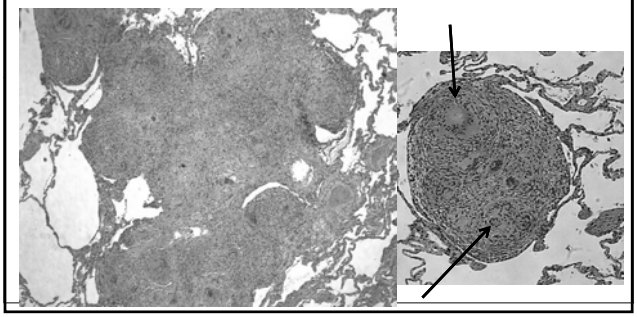
- 42 yo AAM with a past medical history significant for an episode of pericarditis over 10 years prior
- Recently developed symptoms of SOB/DOE and a nonproductive cough
- Some chest discomfort with his shortness of breath but no pleuritic pain, orthopnea or lower extremity edema
- No fevers, chills, night sweats or recent weight changes

- PMHx: Pericarditis, OSA
- PHSx: wrist surgery
- Meds: MVI
- FamHx: unremarkable
- SocHx: Works at a printing warehouse, computer work. No alcohol, tobacco or drug use

- PFTs: Mild restriction and mild reduced DLCO

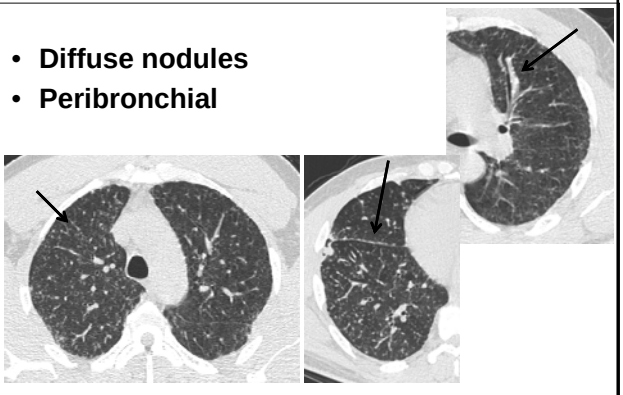
Case #5

- Non-caseating granulomas



Case #5

- Diffuse nodules
- Peribronchial



Sarcoidosis

- Multisystem disease
- Characterized by granulomatous inflammation
- Dyspnea, cough, chest pain are common presenting symptoms
- Radiographically:
  - Hilar, mediastinal lymphadenopathy
  - Interstitial fibrosis or ground glass infiltrates
  - peribronchial infiltrates/thickening
  - Beaded or irregular thickening of the bronchovascular bundles, nodules along bronchi, vessels, and subpleural regions, bronchial wall thickening
- PFTs can show restriction or obstruction

Sarcoidosis

- Diagnosis based on finding granulomatous inflammation in a patient with a compatible clinical history
- Rule out other cause of granulomas
  - Infections such as mycobacterial and fungal infections
  - Beryllium and other metals exposure
  - Granulomas have been identified in reaction to cancer or lymphoma
- Differentiate from granulomas related to hypersensitivity pneumonitis

Sarcoidosis

- Monitoring for other organ involvement
  - Ocular
  - Cardiac

  - Echo: EF 15-20%
  - Cardiac MRI:
    - » Severely dilated LV with severe global hypokinesis. Estimated EF 20%.
    - » Evidence of increased signal intensity suggestive of postinflammatory changes.
    - » Delayed contrast images demonstrate diffuse hyperenhancment suggestive of fibrous replacement scarring.

Sarcoidosis

- Treatment of sarcoidosis usually is based on symptoms and pulmonary function testing
- Absolute indications for therapy include cardiac and neurologic involvement, hypercalcemia, ocular disease
- Therapies include
  - Corticosteroids
  - Hydroxychloroquine
  - Methotrexate
  - Infliximab

Case #6

Case #6

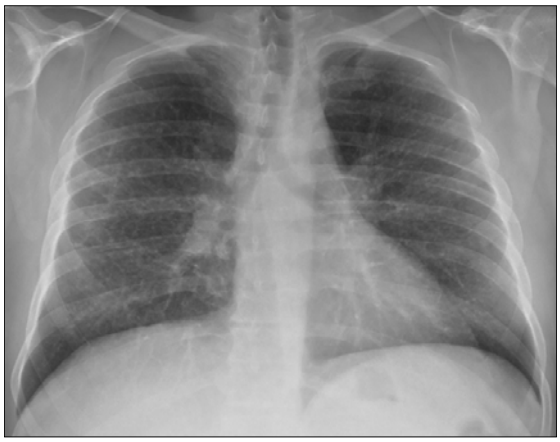
- 48-year old man with 2-year history of dyspnea
- Past medical history: hypertension, gout
- Meds: lisinopril, hydrochlorothiazide, allopurinol
- Family history: negative

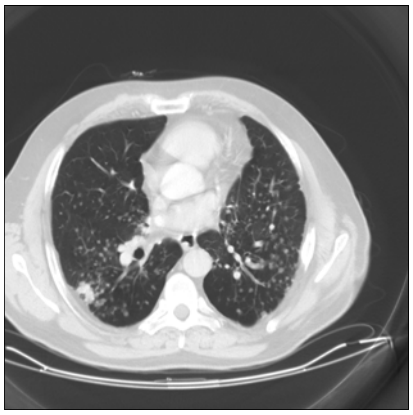
Pulmonary Function Tests

• FVC	4.07 L	91%
• FEV1	3.04 L	87%
• FEV1/FVC		74%
• TLC	5.58 L	91%
• DLCO	21.0	71%

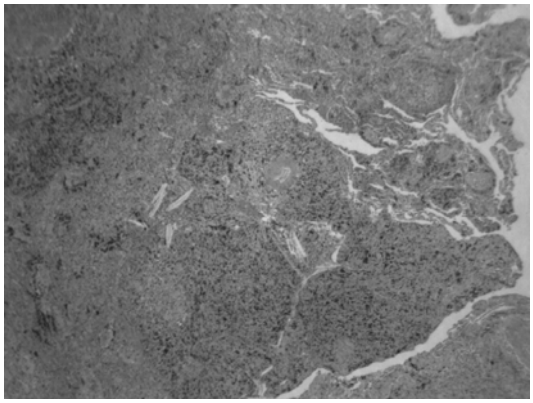
- Low diffusing capacity with normal spirometry and lung volumes

- Social history: worked 30 years in a foundry in cleaning room where he was responsible for chipping and grinding sand off of metal castings. Wore mask occasionally
- 20 pack year smoker
- Exam: lungs clear, no clubbing
- PPD skin test: negative

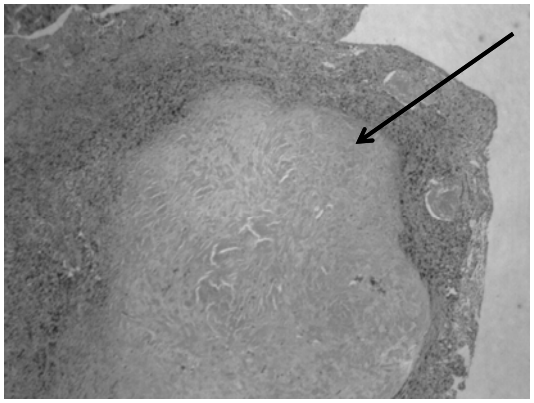




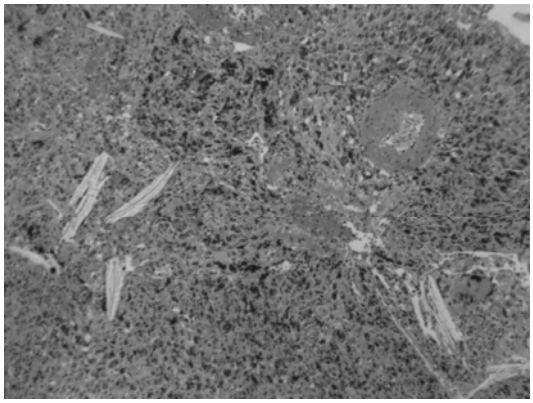
Hundreds of tiny nodules



Granulomatous Infiltrates



Silicotic Nodule

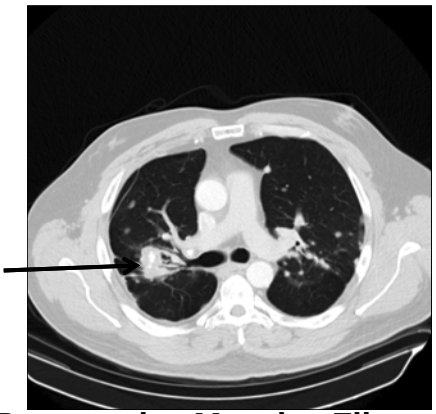


Pigmented Dust and Silica Crystals

Silicosis

- Most common element on surface of the earth
- High risk occupations: miners, quarry workers, sandblasters, foundry workers, many others
- X-ray: upper lobe nodules, lymph node calcification, progressive massive fibrosis
- High risk for TB
- No effective treatment; remove from environment

Case #7



Progressive Massive Fibrosis

Case #7

- 59yo WM with a several month history of SOB and nonproductive cough
- Initially treated with antibiotics, felt better but symptoms recurred. No improvement after second round of antibiotics and inhaler
- CXR with bilateral infiltrates
- Follow up CXR showed some improvement but new infiltrates in other areas

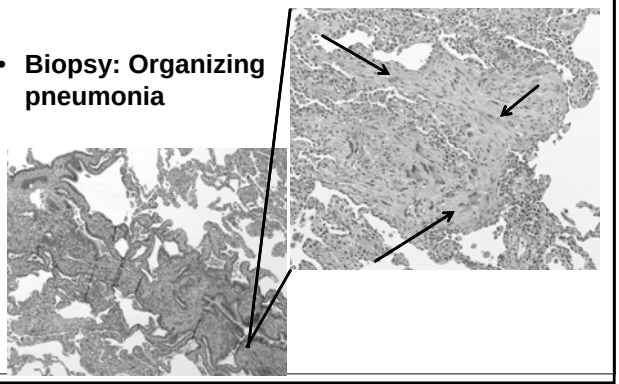
Case #7

- PMHx: pernicious anemia
- Meds: Vitamin B12
- SOCHx: nonsmoker, no exposures

- Exam with crackles and squeaks in the bases

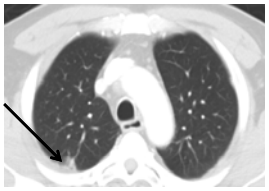
Case #7

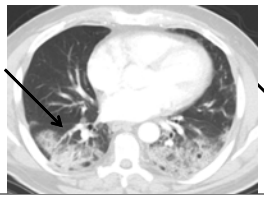
- Biopsy: Organizing pneumonia

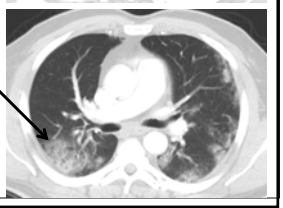


Case #7

- Chest CT:
  - Ground glass infiltrates
  - Nodular lesions







Organizing pneumonia

- Organizing pneumonia is a histologic pattern
- A corresponding clinical-radiologic- pathologic diagnosis

- Organizing pneumonia may result from:
  - Infection by bacteria, viruses, parasites, and fungi
  - Drugs
  - Radiation therapy
  - Clinical conditions
    - » Connective tissue disorders (dermatomyositis, rheumatoid arthritis, Sjogren's syndrome)
    - » Autoimmune processes
    - » Ulcerative colitis, Crohn's
    - » Transplantation: lung, bone marrow
    - » Hematologic malignancies
- If no identifiable cause, cryptogenic organizing pneumonia (COP)
- Bronchiolitis obliterans organizing pneumonia (BOOP)

Organizing pneumonia

- Histologic pattern
  - Nonspecific reaction from alveolar damage with intra-alveolar leakage of plasma proteins
  - Presence of buds of granulation tissue consisting of fibroblasts and myofibroblasts embedded in a connective tissue matrix
  - Present in the lumen of the distal airspaces (the alveoli, alveolar ducts, and bronchioles)
  - Bronchoscopic biopsy or surgical lung biopsy

Cryptogenic Organizing Pneumonia

- Chest imaging shows patchy alveolar opacities, usually bilateral, often migratory
- Can be ground glass, or dense mass-like lesions
- May also present as cavitary lesions, nodules,
- Bronchoscopy shows a ‘‘mixed pattern,’’ with an increase in lymphocytes, neutrophils and eosinophils
- Tissue biopsy required to confirm diagnosis

Cryptogenic Organizing Pneumonia

- Effects men and women equally
- Usually 50-60s yo, not related to smoking
- Initially present with a subacute flu-like syndrome that lasts for a few weeks
- Often accompanied by mild fever, anorexia, weight loss, sweats, nonproductive cough, and mild dyspnea
- Initially thought to be infectious in etiology, no/partial response to antibiotics
- May also have a more severe presentation with features of acute respiratory distress syndrome (ARDS)
- Physical examination, laboratory testing is nonspecific

Cryptogenic Organizing Pneumonia

- Corticosteroids are the standard treatment of COP
- Rapid clinical and imaging response to corticosteroids
- Clinical symptoms improve within days, radiographs show resolution within a few weeks
- Significant number may relapse rates
- In most reports, relapses were not associated with increased mortality or increased long-term functional morbidity
- Did not seem to relate to steroid dose or tapering

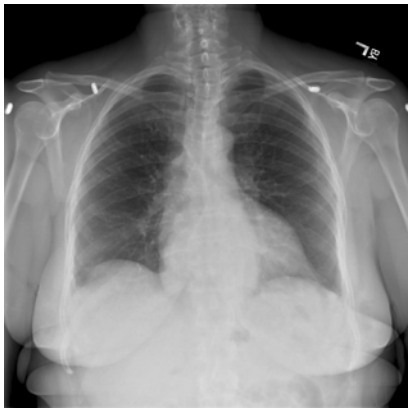
Case #8

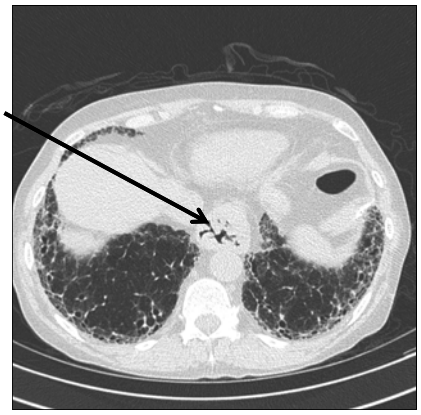
Case #8

- **Exam: basilar crackles; no clubbing**
- **Labs: all autoimmune serology negative**
- **Pulmonary function tests: mild restriction with mild reduction in the diffusing capacity**

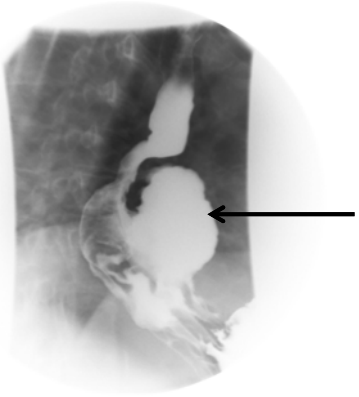
Case #8

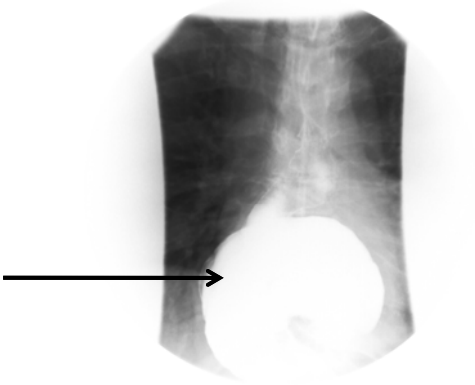
- **73 year old woman with dyspnea for 6 years**
- **Past Medical History: hypertension, hyperlipidemia, hiatal hernia**
- **Social history: retired accountant; rare smoking**
- **Environmental history: no exposures**

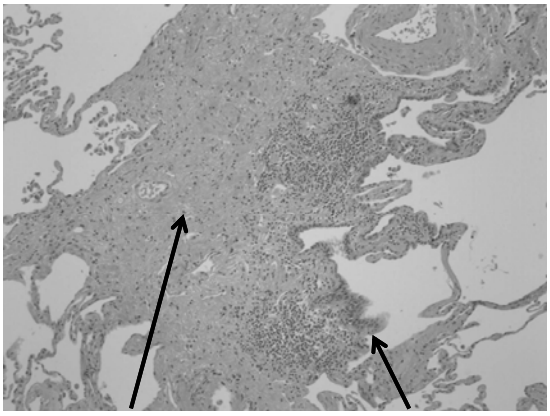




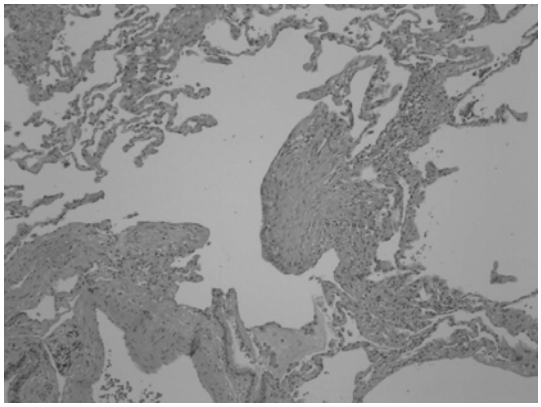
Large Hiatal Hernia







Pulmonary fibrosis Epithelial injury



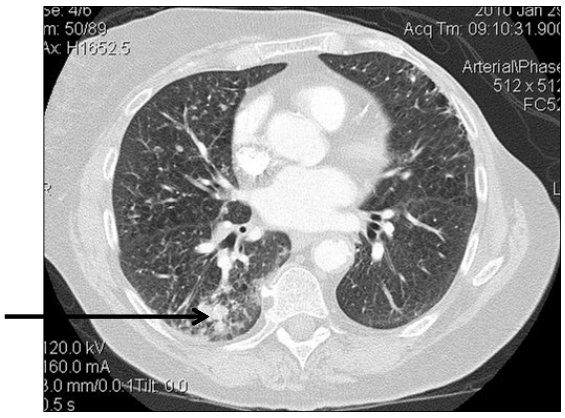
Epithelial injury

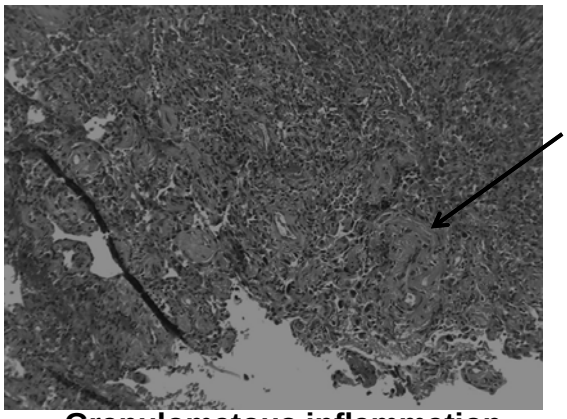
Regurgitation Causing Interstitial Lung Disease

- **69-year old woman with episodic dyspnea x 1 year**
- **Dyspnea episodes accompanied by fever to 102**
- **On-going GERD symptoms with regurgitation of food every 3 days**
- **Exam: bibasilar crackles**

Paraesophageal hernias and interstitial lung disease

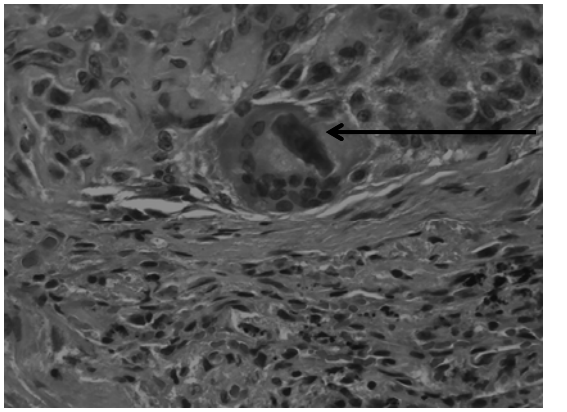
- **Chronic aspiration and/or GERD can result in interstitial lung disease**
- **Consider when patients have aspiration symptoms or hiatal hernia**
- **Prominent epithelial hyperplasia in the setting of few fibroblastic foci are a clue**
- **Treatment is to fix the hernia/GERD**





Granulomatous inflammation

Case #9



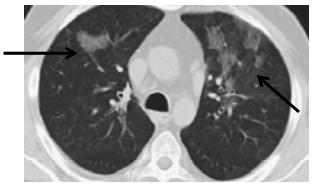
Foreign body in multi-nucleated giant cell

Case #9

- 24yo WF without significant past medical history
- One month prior, developed symptoms of anterior chest discomfort and nonproductive cough
- Symptoms persisted for several weeks, treated with decongestant and cough medication without improvement
- Received an initial round of antibiotics but did not have significant improvement
- CXR showed hazy bilateral infiltrates and she was treated with a second course of antibiotics but remained symptomatic
- No hemoptysis, fevers or chills but some night sweats and weight loss. Increasing SOB/DOE, difficulty climbing stairs.

Case #9

- PMHx (-)
- Meds: recent albuterol inhaler, minocycline for acne, OCP
- SOC: (-) tob, drugs, exposures, travels
- Chest CT:

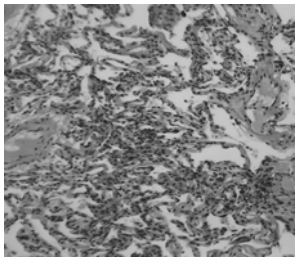


Drug-induced lung disease

- Patterns of drug-induced lung injury
  - Interstitial lung disease
    - » All histopathologic subtypes of interstitial lung disease can be observed as the result of treatments with drugs
  - Alveolar changes
    - » Pulmonary edema, hemorrhage, diffuse alveolar damage, exogenous lipoid pneumonia, alveolar proteinosis
  - Vasculitis

Case #9

- Biopsy: interstitial inflammation and eosinophilia, organizing pneumonia, focal accumulation of foamy macrophages within alveolar lumens
- Minocycline started about 6 weeks prior to symptoms



Drug-induced lung disease

- Difficult to predict
- No reliable clinical, imaging, bronchoalveolar lavage (BAL), or histopathologic feature that is specific of, or diagnostic for drug-induced ILD
- Establish a definite temporal relationship between exposure to the agent and the onset of the lung disease
- Differentiate from cardiac etiology, concomitant ILD, opportunistic infection
- Stop the drug, corticosteroids

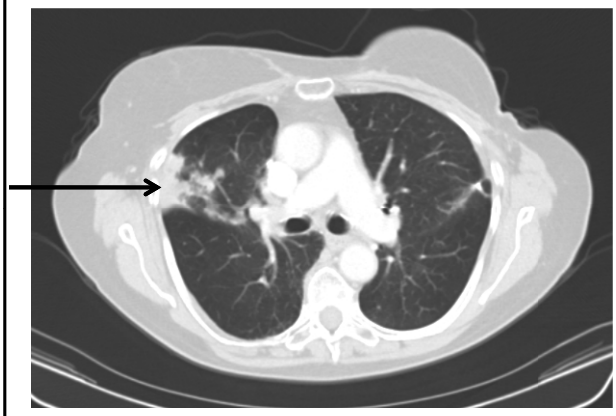
Drug-induced lung disease

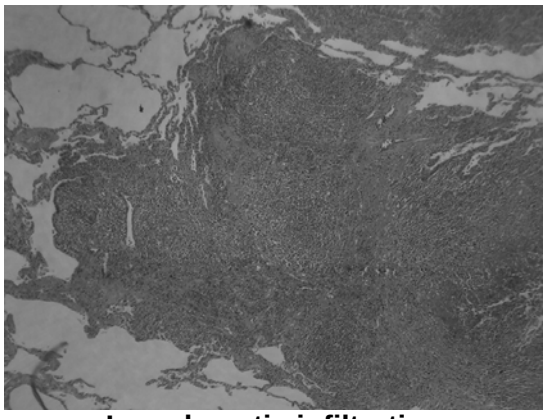
- Common drugs
  - Minocycline
  - Nitorfurantoin
  - Amiodarone
  - Methotrexate
- Pneumotox, www.pneumotox.com

Case #10

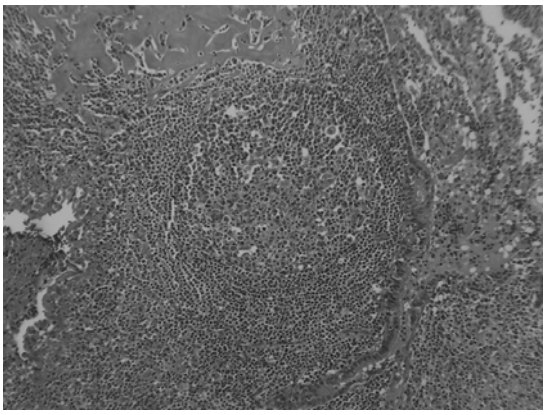
- 58-year old woman
- Cough, fever, and dyspnea for 2 months
- Used hot tub daily because of arthritis
- Admitted and diagnosed with pneumonia
- Improved with empiric antibiotics
- Symptoms recurred after returning home from the hospital

Case #10

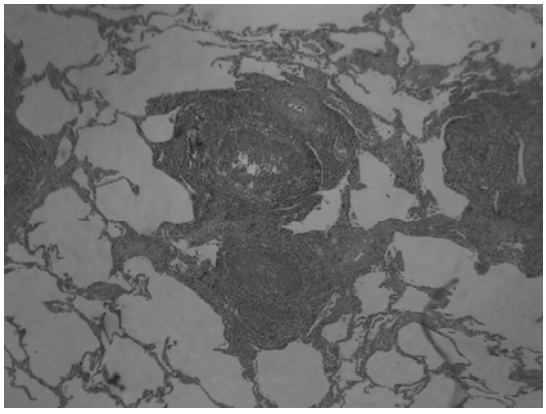




Lymphocytic infiltration



Necrotizing granulomas



Lymphocytic infiltration around airways

Culture = Mycobacterium avium complex

Hot Tub Lung

- Causes:
  - Mycobacterium avium complex
  - Hypersensitivity pneumonitis
- Treatment:
  - Avoidance
  - Steroids for severe cases
  - Occasionally antibiotics:
    - Clarithromycin
    - Rifampin
    - Ethambutol

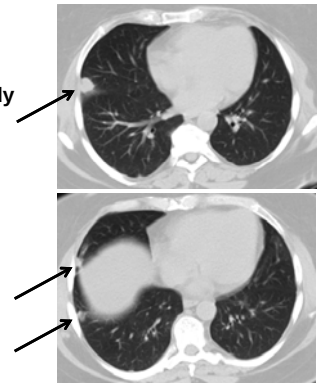
Case #11

Case #11

- 54 yo WM with a history of shortness of breath and cough that has been present for 6 months and a CXR showing a lung mass.
- Originally presented to his PCP with recurrent sinus infections, epistaxis and was treated with a number of antibiotics. A CXR and CT showed pulmonary nodules.
- He notes SOB/DOE, fatigue, sinus congestion and drainage with a dry cough.
- PMHx: chronic sinusitis; Hypertension
- Meds: MVI, guaifenesin, amlodipine, atenolol, lisinopril-hydrochlorothiazide, Nexium, meloxicam, nasonex, and clindamycin
- SOCHx: Former smoker, 25PY, drinks alcohol, no illicit drugs
- Occupation: Construction worker with exposure to pesticides, asbestos, dust and mold

Case #11

- Normal chemistries, CBC
- Normal urinalysis
- (+) ANCA, (+) PR3 antibody
  (-) ANA, RF
- Chest CT: multiple pulmonary nodules

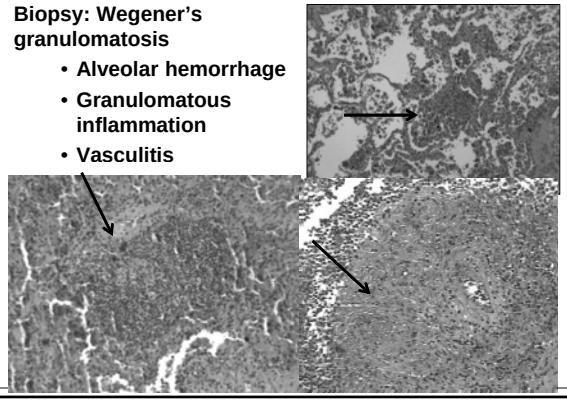


Wegener's Granulomatosis

- WG is the most common of the small-vessel vasculitis, associated with antineutrophil cytoplasmic antibody (ANCA)
- Characterized by
  - Upper and lower respiratory tract involvement
    - » Most common manifestations of WG, especially at the time of onset of the disease
  - Upper airway disease can include:
    - » Epistaxis, rhinitis, sinusitis, deforming or ulcerating upper airway lesions, otitis, otalgia, tinnitus, hearing loss, laryngeal disease, subglottic stenosis, and/or tracheal stenosis
  - Lower respiratory disease includes: cough, chest pain, shortness of breath, hemoptysis

Wegener's Granulomatosis

- Biopsy: Wegener's granulomatosis
  - Alveolar hemorrhage
  - Granulomatous inflammation
  - Vasculitis



Wegener's Granulomatosis

- Subglottic, tracheal, and endobronchial disease usually not present at the time of diagnosis, but often develops after a delay of months or years
- Renal involvement is present in 40% of patients at the time of initial presentation but develops in 70% to 80% of patients over the course of the disease
- Other target organs can include:
  - Skin
  - Eyes
  - Peripheral nervous system
  - Musculoskeletal system
  - Heart

Wegener's Granulomatosis

- Present with target organ specific symptoms
- Constitutional symptoms are common, most patients have fatigue malaise, anorexia, fever, or weight loss
- Chest imaging shows interstitial, alveolar or mixed infiltrates, nodules, or cavities
- Pathologically, characterized by a necrotizing, small- and medium-vessel vasculitis, granulomatous inflammation

Wegener's Granulomatosis

- Treatement
  - Initial induction of remission with immunosuppression
    - » Consists of cyclophopshamide and glucocorticoids
    - » Rituximab can be used if cannot use cyclophosphamide
  - Maintenance immunosuppressive therapy to prevent relapse
    - » Less toxic regiment with azathioprine or methotrexate
    - » Concurrent glucocorticoids

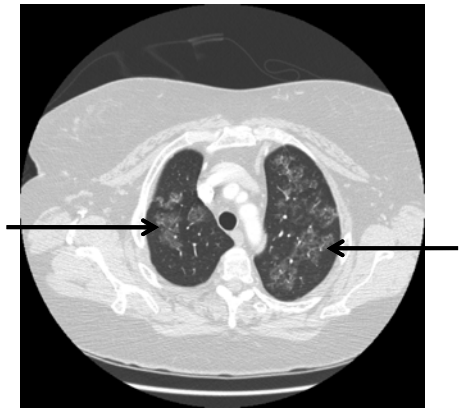
Wegener's Granulomatosis

- Diagnosis confirmed by tissue biopsy at a site of active disease
  - Skin biopsy of the skin shows leukocytoclastic vasculitis with little or no complement and immunoglobulin on immunofluorescence
  - Renal biopsies in patients with signs of renal disease and active urine sediment
  - Lung biopsy usually requires a surgical biopsy showing pulmonary capillaritis, granulomatous inflammation may be seen, exclude infections

Case #12

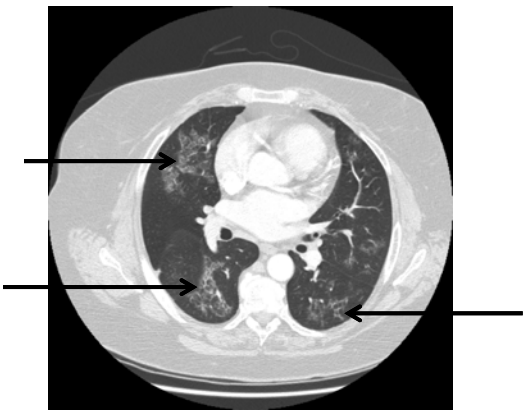
Case #12

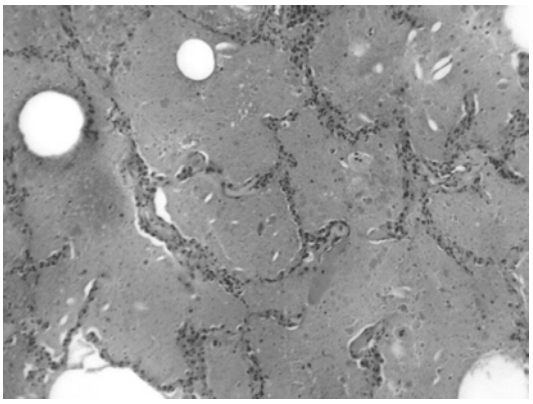
- 58-year old woman with 6 month history of dyspnea
- CXR showed pulmonary infiltrates but there was no improvement after empiric antibiotics
- PMH: hypothyroidism
- FHX: negative
- Exam: lung clear; no clubbing



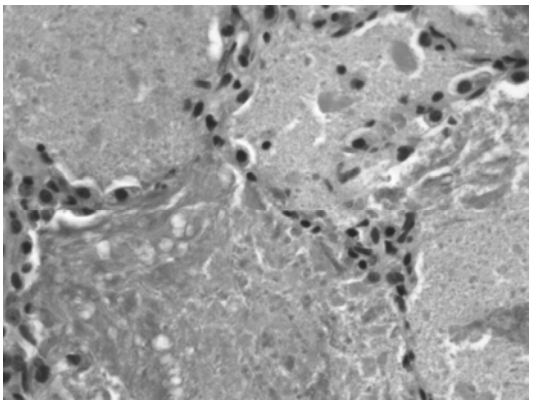
Pulmonary Function Tests

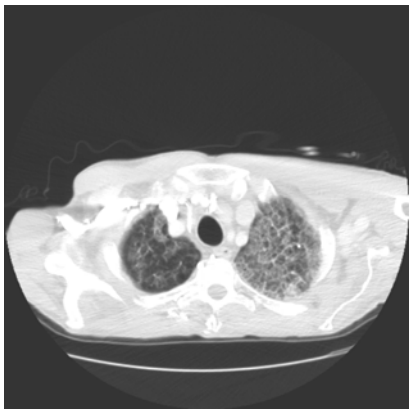
• FVC	2.94	109%
• FEV1	2.31	104%
• FEV1/FVC	77%	
• TLC	4.20	91%
• DLCO	14.9	72%

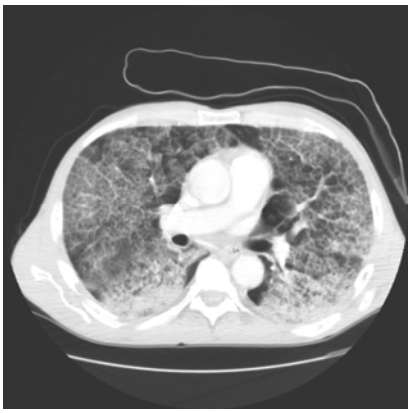


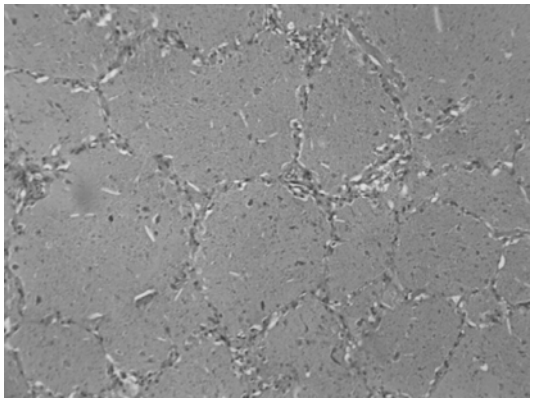


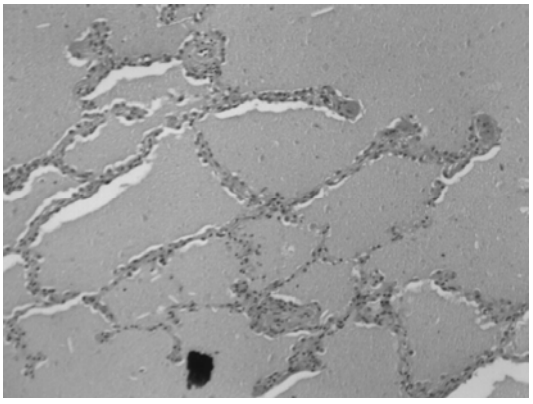
- **63-year old man with progressive dyspnea and hypoxemia over 3 months**
- **Underwent stem cell transplant for lymphoma 8 months earlier**











Pulmonary Alveolar Proteinosis

- **Accumulation of surfactant lipid and protein in alveolar spaces**
- **Causes:**
  - **Congenital: abnormal surfactant or GM-CSF receptors**
  - **Acquired: GM-CSF antibodies**
  - **Secondary: following massive dust inhalation, bone marrow transplant, or with leukemia/lymphoma**

Pulmonary Alveolar Proteinosis

- **Diagnosis:**
  - **Brownish fluid on bronchoalveolar lavage**
  - **Biopsy = PAS positive material in alveoli**
- **Treatment:**
  - **Observation**
  - **Whole lung lavage**
  - **GM-CSF?**