Interstitial Lung Disease

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ILD Classification
Connective Tissue Diseases
- Scleroderma
- Polymyositis-Dermatomyositis
- Systemic Lupus Erythematosus
- Rheumatoid Arthritis
- Mixed Connective Tissue Disease
- Ankylosing Spondylitis

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, penicillamine
- 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 interstitial pneumonitis
- Respiratory bronchiolitis
- Cryptogenic organizing pneumonia
- Nonspecific interstitial pneumonitis
- Lymphocytic interstitial pneumonia (Sjogren’s 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 Erythematosus (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 pneumoconiosis

AA 10-12x more often seen with Sarcoidosis
Pathophysiology of ILD

The **diaphragm** is a muscle below the lungs. It flattens to draw air in as you inhale, then rises as you exhale.

**Bronchioles** are the smallest airways.

**Alveoli** are air sacs at the ends of the bronchioles.

**Blood vessels** surround the alveoli.

**Damaged alveoli** supply less oxygen to the body.

**CO₂** and **O₂** are exchanged between the blood and air in the alveoli.

**Scarred interstitium** indicates tissue damage.

Inside blood vessel

Inside alveoli

Interstitium
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
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
CHF

Pneumothorax
### HRCT Findings with ILD

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

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

- **Left pulm. a**
- **PDA**
- **Desc. aorta**
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

<table>
<thead>
<tr>
<th></th>
<th>Predicted Value</th>
<th>Observed Pre</th>
<th>%Pred</th>
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<tbody>
<tr>
<td><strong>SPIROMETRY</strong></td>
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<tr>
<td>FVC</td>
<td>2.75</td>
<td>1.52*</td>
<td>55</td>
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<tr>
<td>FEV1</td>
<td>2.17</td>
<td>1.14*</td>
<td>52</td>
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<tr>
<td>FEV1/FVC</td>
<td>77</td>
<td>75</td>
<td>97</td>
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<tr>
<td>FEF25-75%</td>
<td>2.13</td>
<td>.85*</td>
<td>39</td>
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<tr>
<td>PEFR</td>
<td>5.41</td>
<td>3.57*</td>
<td>65</td>
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<tr>
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<td>6.13</td>
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</tr>
<tr>
<td>FVC</td>
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<td>1.43</td>
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<tr>
<td>PIFR</td>
<td>3.6</td>
<td>2.1*</td>
<td>58</td>
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| **LUNG VOLUMES** |                 |              |       |
| SVC             | 2.75            | 1.57*        | 57    |
| IC              | 2.06            | 1.16*        | 56    |
| ERV             | .69             | .41*         | 59    |
| FRC             | 2.79            | 1.88         | 67    |
| RV              | 2.1             | 1.47         | 70    |
| TLC             | 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

<table>
<thead>
<tr>
<th>Antibiotics</th>
<th>Drug-induced systemic lupus erythematosus</th>
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<tbody>
<tr>
<td>Nitrofurantoin, acute and chronic</td>
<td>Procaainamide hydrochloride</td>
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<tr>
<td>Sulfasalazine</td>
<td>Isoniazid</td>
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<td>Minocycline</td>
<td>Hydralazine hydrochloride</td>
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<td>Ethambutol</td>
<td>The hydantoins</td>
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<td></td>
<td>Penicillamine</td>
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<td><strong>Anti-inflammatory agents</strong></td>
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<tr>
<td>Gold</td>
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<td>Penicillamine</td>
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<td>Nonsteroidal antinflammatory agents</td>
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<td><strong>Anti-arrhythmic agents</strong></td>
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<td>Tocainide</td>
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<td>Amiodarone</td>
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<td><strong>Chemotherapeutic agents</strong></td>
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<td>Antibiotics</td>
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<td>Bleomycin sulfate</td>
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<td>Mitomycin C</td>
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<td>Busulfan</td>
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<td>Cyclophosphamide</td>
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<td>Chlorambucil</td>
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<td>Melphalan</td>
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<td>Procarbazine hydrochloride</td>
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<td>Antimetabolites</td>
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<td>Azathioprine</td>
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<td>Cytosine arabinoside</td>
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<td>Methotrexate</td>
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<td>Nitrosoureas</td>
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<tr>
<td>BCNU (carmustine)</td>
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<td>CCNU (lomustine)</td>
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<tr>
<td>Methyl-CCNU (semustine)</td>
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<tr>
<td>Other</td>
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<tr>
<td>Etoposide (VP-16)</td>
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<tr>
<td>Paclitaxel</td>
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<td>Docetaxel</td>
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<td>Thalidomide</td>
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<td>Nilutamide</td>
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<td>Alpha interferon</td>
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<td>Gefitinib</td>
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<td><strong>Miscellaneous</strong></td>
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<tr>
<td>Oxygen</td>
<td>Drugs inducing pulmonary infiltrates and eosinophilia</td>
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<td>Radiation</td>
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<td>L-tryptophan</td>
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<tr>
<td>Bromocriptine</td>
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<tr>
<td>Bacille Calmette-Guerin (BCG)</td>
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Genetically Susceptible
  Multiple or aggressive underlying illness
  immunocompromised

Genetically Pre-disposition
  May present 10yrs earlier in offspring

Autosomal dominant

Family History
CBC
BMP
LFT
RF, ANA, ANCA, Hypersensitivity panel, anti-GBM
Not done: CRP; ESR (not sensitive enough)

Labs and Pathology
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
- Subsegmental bronchi: 3rd order
- Sub-subsegmental bronchi: 4th order
- 5th order: B'alpha • B'alpha

Diagram:
1. Right B'alpha
   - B'beta
   - B'alpha
2. Intermediate bronchus
   - Middle lobe
3. Right middle lobe bronchus
   - B'alpha
   - B'beta
4. Right B'alpha
   - B'beta
   - B'alpha
   - B'beta
   - B'beta
5. Bifurcation of trachea
6. Left inferior lobe bronchus
7. Left B'alpha
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, therapeutic 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