Multidisciplinary Approach to Interstitial Lung Diseases
Case Study: Mr. D.S
Mr. D.S

• 64 YEAR OLD MALE
• SLOWLY PROGRESSIVE COUGH AND DYSPNEA OVER LAST FEW YEARS, MORE FOR THE LAST ONE YEAR
• BASILAR CRACKLES ON EXAM
• CXR SHOWED INTERSTITIAL OPACITIES
• REFERRED TO YOUR CLINIC FOR A FORMAL EVALUATION
Broad/Simplistic categories of ILDs

Interstitial Lung Diseases

- Idiopathic Pulmonary Fibrosis
- Other ILDs
Survival differs in ILDs

Park et al. AJRCCM 2007
Treatment of non-IPF related ILDs

IMMUNOSUPPRESSIVE/CYTOTOXIC MEDICATIONS ARE USEFUL IN TREATING NON-IPF ILDS INCLUDING CRYPTOGENIC ORGANIZING PNEUMONIA, HYPERSENSITIVITY PNEUMONITIS, CONNECTIVE TISSUE ASSOCIATED ILD ETC.

- Corticosteroids
- Azathioprine
- Mycophenolate
- Cyclophosphamide
- Others
Patients with IPF should generally not be treated chronically with corticosteroids
Patients with IPF on prednisone and azathioprine are more likely to die or be hospitalized than those on placebo.

IPF Network NEJM 2012
Nintedanib reduces rate of FVC decline in IPF patients

Richeldi et al. NEJM May 2014

Stanford University
Pirfenidone reduces the rate of decline of FVC
Mr. D.S

- 64 YEAR OLD MALE
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- BASILAR CRACKLES ON EXAM
- CXR SHOWED INTERSTITIAL OPACITIES
- REFERRED TO YOUR CLINIC FOR A FORMAL EVALUATION
Clinical Context + HRCT pattern

E.g., certain cases of IPF, CTD-ILD, HP etc.

Diag nostic

Bronchoscopy, BAL and biopsy (in selected cases)

Not Diagnostic

Surgical Lung Biopsy

Not Diagnostic

Multi-disciplinary discussion

Not Diagnostic

Treat, follow, and revisit diagnosis as necessary
Clinical exam is THE most important tool in the diagnosis of Interstitial Lung Diseases
ILD from one etiology can present with different radiologic and histopathologic patterns.
ILDs from different etiologies share the same radiologic and histopathologic patterns

**Radiologic Patterns**

- CTD ILD
- HP
- UIP Pattern
- IPF
- Drugs

**Histopathologic Patterns**

- CTD ILD
- HP
- UIP Pattern
- IPF
- Drugs
ILD Questionnaires

Date: ___________________________ Name: ___________________________ MR# ______________

Stanford University Medical Center
Center for Interstitial Lung Disease: New Patient Questionnaire
Radiographs and other workup as indicated

**SEROLOGIC TESTING**
- Rheumatoid factor
- Anti-Scl 70
- Etc.

**FORMAL RHEUMATOLOGY CONSULTATION**
Inhalational Exposures (Hypersensitivity Pneumonitis)

<table>
<thead>
<tr>
<th>Agent*</th>
<th>Source</th>
<th>Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minimolds</td>
<td></td>
<td></td>
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<tr>
<td>Thermophilic actinomycetes</td>
<td>Moldy plant materials</td>
<td>Farmer’s lung</td>
</tr>
<tr>
<td>Scopularia torvatae (Microsporum jacta)</td>
<td>Moldy hay</td>
<td>Farmer’s lung, mushroom-worker’s lung</td>
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<tr>
<td>Thermononaspora volcanii</td>
<td>Moldy bag, compost</td>
<td>Farmer’s lung, mushroom-worker’s lung</td>
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<tr>
<td>Bacillus subtilis</td>
<td>Dehydrated enzymes</td>
<td>Dehydrator worker’s lung</td>
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<tr>
<td>Aspergillus clavatus</td>
<td>Moldy grains</td>
<td>Mill-worker’s lung</td>
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<tr>
<td>Aspergillus terreus</td>
<td>Animal bedding</td>
<td>Dog house disease</td>
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<tr>
<td>Aspergillus fumigatus</td>
<td>Tobacco mold</td>
<td>Tobacco-worker’s lung</td>
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<tr>
<td>Penicillium casei</td>
<td>Chalk mold</td>
<td>Chalk-worker’s lung</td>
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<tr>
<td>Penicillium frequentans</td>
<td>Moldy cork</td>
<td>Suberosis</td>
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<tr>
<td>Penicillium chrysogenum</td>
<td>Moldy wood dust</td>
<td>Woodworker’s lung</td>
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<td>Cladosporium corticola</td>
<td>Moldy maple bark</td>
<td>Maple-bark-upper’s lung</td>
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<td>Aspergillus palustris</td>
<td>Moldy sugar dust</td>
<td>Sequinian</td>
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<td>Aspergillus species</td>
<td>Contaminated water</td>
<td>Sulfonamide’s disease</td>
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<tr>
<td>Alternaria species</td>
<td>Wood or wood pulp</td>
<td>Woodworker’s lung</td>
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<tr>
<td>Metallos, lye reemans</td>
<td>Dry rot lung</td>
<td></td>
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<tr>
<td>Bacillus subtilis</td>
<td>Grape mold</td>
<td>Winesower’s lung or Spilacid lung</td>
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<tr>
<td>Talaromyces autotrophicus</td>
<td>Mold in Japanese homes</td>
<td>Screen type HP</td>
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<tr>
<td>Cladosporium sp.</td>
<td>Sawyer</td>
<td>Sawyer-worker’s lung</td>
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<tr>
<td>Mucor mucedo</td>
<td>Papula</td>
<td>Papula-corner’s lung</td>
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<tr>
<td>Candida albicans</td>
<td>Thermostable respirot</td>
<td>Box lung</td>
</tr>
<tr>
<td>Myrothecium avricanum-euschnii</td>
<td>Contaminated water</td>
<td>Box sub lung</td>
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<tr>
<td>Mite, mite motus, and bacteria</td>
<td>Cold mist and other humidities, air conditioners</td>
<td>Yellow plant or office worker or air conditioners’ lung, ventilation pneumonia</td>
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<tr>
<td>Bacteria and fungi</td>
<td>Contaminated metal-working fluids</td>
<td>Machine-operator’s lung</td>
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<tr>
<td>Anaerobes</td>
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<tr>
<td>Rat proteins</td>
<td>Bird excreta, blood or feather</td>
<td>Bird-breeders lung, bird-fancier’s lung, pigeon-breeder’s lung</td>
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<tr>
<td>Gnotobiotics</td>
<td>Rat, mouse or guinea pig</td>
<td>Rodent handler’s lung</td>
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<td>Germi</td>
<td>Germi-breeder’s lung</td>
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<tr>
<td>Ox and pork proteins</td>
<td>Animal fur</td>
<td>Farmer’s lung</td>
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<tr>
<td>Melibokus wellirensis</td>
<td>Primary staff</td>
<td>Primary staff’s lung</td>
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<tr>
<td>Fish</td>
<td>Melibokus shell dust</td>
<td>Orange shell lung</td>
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<tr>
<td>Wheat meal</td>
<td>Fish meal dust</td>
<td>Fishmeal-worker’s lung</td>
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<tr>
<td>Silk woven sari proteins</td>
<td>Flour</td>
<td>Miller’s lung</td>
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<td>Plants</td>
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<td>Soybean hull</td>
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<td>Coffee</td>
<td>Coffee bean dust</td>
<td>Coffee-worker’s lung</td>
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<td>Lycopersicum species</td>
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<td>Lycopersicon</td>
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<tr>
<td>Incoponates</td>
<td>Plastics</td>
<td>Paint-refinisher’s lung</td>
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<td>Antifungal</td>
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<tr>
<td>Psoralen</td>
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<td>Psoralens</td>
<td></td>
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<tr>
<td>Pyrethrum</td>
<td>Insecticides</td>
<td>Insecticide lung</td>
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<tr>
<td>Metals</td>
<td></td>
<td></td>
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<tr>
<td>Cobalt</td>
<td></td>
<td>Hard metal lung</td>
</tr>
<tr>
<td>Beryllium</td>
<td></td>
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</tbody>
</table>

*The more frequent causative agents are listed in bold type.
Medications and Occupations

**OCCUPATIONAL LUNG DISEASES**
- Occupational history
- ALL occupations

**DRUGS**
- Common drugs
  - Nitrofurantoin
  - Methotrexate
  - Amiodarone
  - Etc.

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Stanford University
Mr. D.S: Additional history

- Smoked 1 pack/day until 15 years ago
- Intermittent woodworking, but now wears mask
- Some mold in bathroom in home but otherwise no significant mold infestation
- Down clothing and bedding at home
- No diagnosis of a connective tissue disease but complaints of joint pain in hands and feet without associate swelling
- Physical exam did not show any evidence of active or past connective tissue disease
Mr. D.S: Working Diagnostic Considerations

- **Idiopathic Pulmonary Fibrosis**
- **Chronic Hypersensitivity Pneumonitis**
- **Rheumatoid Arthritis Associated Connective Tissue Disease**
Mr. D.S

- The CRP, ESR, ANA, Anti Scl 70, SSA, SSB, Myositis panel were all negative except for slight elevation in RF and a positive Anti CCP
Clinical Context + HRCT pattern

E.g., certain cases of IPF, CTD-ILD, HP etc.

Diagnostic

 Bronchoscopy, BAL and biopsy (in selected cases)

Not Diagnostic

Surgical Lung Biopsy

Not Diagnostic

Multi-disciplinary discussion

Not Diagnostic

Treat, follow, and revisit diagnosis as necessary

Raj et al. Chest 2016
Clinical Context + HRCT pattern

E.g., certain cases of IPF, CTD-ILD, HP etc.

Diagnostic

Bronchoscopy, BAL and biopsy (in selected cases)

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Surgical Lung Biopsy

Not Diagnostic

Multi-disciplinary discussion

Not Diagnostic

Treat, follow, and revisit diagnosis as necessary
HIGH RESOLUTION CT CHEST

VARIOUS PATTERNS
CT Chest: Usual Interstitial Pneumonia Pattern

CT Chest: Probable Usual Interstitial Pneumonia Pattern

CT Chest: Indeterminate Pattern
CT Chest: Alternative Diagnosis Pattern

HIGH RESOLUTION CT CHEST

INTERSTITIAL LUNG DISEASE PROTOCOL
Conventional vs High Resolution CT
Prone vs. Supine Images
Air trapping is better appreciated on expiratory images.
Mr. D.S: HRCT Images
Mr. D.S: HRCT Images
Mr. D.S: HRCT Images

[Images of HRCT scans of the chest]
Mr. D.S:

- **CT Chest showed an indeterminate UIP pattern**
- **Not helpful in narrowing the differential diagnosis**
Mr. D.S: Working Diagnostic Considerations

- **Idiopathic Pulmonary Fibrosis**
- **Chronic Hypersensitivity Pneumonitis**
- **Rheumatoid Arthritis Associated Connective Tissue Disease**
Mr. D.S:

- REFERRED TO RHEUMATOLOGY
- THE PATIENT DID NOT MEET CRITERIA FOR CONNECTIVE TISSUE DISEASE AND RHEUM RECOMMENDED TO DIAGNOSE AND TREAT THE ILD AS IF IT WAS NOT RELATED TO A CONNECTIVE TISSUE DISEASE
Clinical Context + HRCT pattern

- Diagnostic
  - E.g., certain cases of IPF, CTD-ILD, HP etc.
  - Bronchoscopy, BAL and biopsy (in selected cases)
    - Not Diagnostic
      - Diagnostic
      - Surgical Lung Biopsy
        - Not Diagnostic
          - Multi-disciplinary discussion

Treat, follow, and revisit diagnosis as necessary
Bronchoscopy, lavage and biopsy
Clinical Context + HRCT pattern

E.g., certain cases of IPF, CTD-ILD, HP etc.

- Diagnostic
  - Bronchoscopy, BAL and biopsy (in selected cases)
    - Not Diagnostic
      - Not Diagnostic
        - Surgical Lung Biopsy
          - Not Diagnostic
            - Not Diagnostic
              - Multi-disciplinary discussion
                - Treat, follow, and revisit diagnosis as necessary

Treat, follow, and revisit diagnosis as necessary
Surgical Lung Biopsy

Thoracoscopic (VATS) Lung Biopsy
- 3 incisions (5-10 mm)
- Access to all aspect of the chest
- Favored approach if patients will tolerate anesthesia

Postoperative Care
- Chest tube in place (overnight)
- Majority are home in 1-2 days (>90% in our practice)
- Primary concern is air leak
Mortality following surgical lung biopsy

Raj et al. Chest 2016

Stanford University
Mr. D.S:

- **REFERRED FOR A SURGICAL LUNG BIOPSY (VATS)**
- **UNEVENTFUL PROCEDURE AND RECOVERY**
Mr. D.S: Surgical Lung Biopsy
Clinical Context + HRCT pattern

- E.g., certain cases of IPF, CTD-ILD, HP etc.

- Diagnostic

- Bronchoscopy, BAL and biopsy (in selected cases)
  - Not Diagnostic

- Not Diagnostic

- Surgical Lung Biopsy
  - Not Diagnostic

- Not Diagnostic

- Multi-disciplinary discussion

- Treat, follow, and revisit diagnosis as necessary
Agreement on the final diagnosis increases with multidisciplinary discussion.

91 ILD PATIENTS

**STEP 1**
- Expert clinicians and radiologists independently reviewed HRCT
- Opinion: Definite, probable, possible and not UIP

**STEP 2**
- Clinicians and radiologists reviewed HRCT with clinical information
- No discussion between participants

**STEP 3**
- Clinician and radiology conference; discussed results with each other

**STEP 4**
- Conference: Clinicians, radiologists and pathologists discussing cases and their diagnoses

**STEP 5**
- All discussants tried to reach a consensus diagnosis

Flaherty et al. AJRCCM 2004
Stanford Multidisciplinary Interstitial Lung Disease Conference

- PULMONARY MEDICINE
- THORACIC RADIOLOGY
- PULMONARY PATHOLOGY
- RHEUMATOLOGY
- LUNG TRANSPLANT
- THORACIC SURGERY
- CLINICAL RESEARCH
Mr. D.S: Final Diagnosis

Consensus Multidisciplinary Diagnosis: Idiopathic Pulmonary Fibrosis
Clinical Context + HRCT pattern

- Diagnostic
  - E.g., certain cases of IPF, CTD-ILD, HP etc.
  - Bronchoscopy, BAL and biopsy (in selected cases)
  - Surgical Lung Biopsy
    - Not Diagnostic
    - Multi-disciplinary discussion
    - Not Diagnostic
  - Treat, follow, and revisit diagnosis as necessary
Mr. D.S: Clinical Course

- **Started on Anti-Fibrotic Medications**
- **Tolerated well except for mild and manageable symptoms**
Mr. D.S: Clinical Course

Qualified for, and enrolled in a trial for novel therapeutic agent for idiopathic pulmonary fibrosis.
Mr. D.S: Clinical Course

- Stable for 3 years, and then progressed clinically
- Received a double lung transplant and doing well 1 year postoperatively
Questions