**Interstitial Lung Disease 2007**

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**ILD: Definition**

1. ILD is not one disorder
2. Strictly speaking, an ILD involves the interstitium  
   Anatomic structures other than the interstitium can be involved  
   “alveolitis”  
   “vasculitis”  
   “peri-bronchial disease”

**What Conditions Belong to “ILD”?**

1. Diffuse abnormalities on chest radiology  
   “Diffuse Parenchymal Lung Disease” (DPLD) is the more general and preferred term.
2. Similar clinical presentations
3. Similar physiological consequences
4. Generally, chronic non-infectious, non-neoplastic disease involving the lung parenchyma.

**ILD: Thickening of the Interstitium**

**ILD: Cellular and Fibrotic**

Slides Courtesy of Alain Borczuk, MD
Classification of Diffuse Parenchymal Lung Disease

Systemic Disease

DPLD

Classification of Diffuse Parenchymal Lung Disease

Systemic Disease

Known Cause & Other

Drugs

Pneumoconioses

Eosinophilic granuloma


Classification of Diffuse Parenchymal Lung Disease

Systemic Disease

Granulomatous

Sarcoid

Chronic hypersensitivity pneumonitis

Drugs

Pneumoconioses

EG


Classification of Diffuse Parenchymal Lung Disease

Systemic Disease

Granulomatous

Idiopathic Interstitial Pneumonia (IIP)

Drugs

Pneumoconioses

EG


Classification of Diffuse Parenchymal Lung Disease

Systemic Disease

Non-UIP

UIP (IPF)

Cellular Fibrotic

NSIP


Survival for UIP vs NSIP

Years

Alive (%)

UIP

NSIP

Others


**COMPARATIVE MORTALITY RATES**

<table>
<thead>
<tr>
<th>DISEASE</th>
<th>5-YEAR MORTALITY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung Cancer</td>
<td>85%</td>
</tr>
<tr>
<td>IPF</td>
<td>50-70%</td>
</tr>
<tr>
<td>CHF</td>
<td>50%</td>
</tr>
<tr>
<td>Colorectal Cancer</td>
<td>38%</td>
</tr>
<tr>
<td>Breast Cancer</td>
<td>13%</td>
</tr>
<tr>
<td>Prostate Cancer</td>
<td>2%</td>
</tr>
</tbody>
</table>

**Prevalence of ILD**

<table>
<thead>
<tr>
<th>occupational/Environmental</th>
<th>MALE</th>
<th>FEMALE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug &amp; Radiation</td>
<td>1.2</td>
<td>2.2</td>
</tr>
<tr>
<td>Rheumatologic</td>
<td>7.1</td>
<td>11.6</td>
</tr>
<tr>
<td>IPF</td>
<td>20.2</td>
<td>13.2</td>
</tr>
<tr>
<td>Pulm Fibrosis (Not IPF)</td>
<td>10.1</td>
<td>14.3</td>
</tr>
<tr>
<td>Sarcoidosis</td>
<td>8.3</td>
<td>8.8</td>
</tr>
</tbody>
</table>

*Am J Respir Crit Care Med 1994; 150: 967-972.*

**Epidemiology of IPF**

- **Incidence**
  - Estimated 31,000 New Patients per Year in the United States

- **Prevalence**
  - Estimated 33,000 Current Patients in the United States

**ILD: CLINICAL HISTORY**

- Insidious onset
- Preceding URI
- Occupational Exposure and Cigarette Smoking
- Progressive Dyspnea with Exertion (DOE)
- Paroxysmal cough

**ILD: PHYSICAL FINDINGS**

- Tachypnea
- Basilar crackles
- May have digital clubbing
- Low lung volume, cyanosis, tachycardia

**ILD: PHYSIOLOGIC FINDINGS**

- Pulmonary function
  - Restrictive ventilatory defect
    - Reduced total lung capacity (TLC) & FVC
    - Normal or increased FEV1/FVC ratio
  - Impaired gas exchange
    - Decreased DLCO
    - Desaturation with exercise (pulse oxymetry)
    - Decreased PaCO2
    - Increased A-a gradient

Adapted from ATS/ERS. Am J Respir Crit Care Med. 2002;166:664-666.
**Pulmonary Function Testing**

**Examples:**

<table>
<thead>
<tr>
<th></th>
<th>Obstructive</th>
<th>Restrictive</th>
<th>Normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVC</td>
<td>100%</td>
<td>50%</td>
<td>&gt;70%</td>
</tr>
<tr>
<td>FEV1</td>
<td>50%</td>
<td>50%</td>
<td>&gt;80%</td>
</tr>
<tr>
<td>FEV1/FVC</td>
<td>43%</td>
<td>90%</td>
<td>&gt;70%</td>
</tr>
<tr>
<td>TLC</td>
<td>100%</td>
<td>65%</td>
<td>&gt;80%</td>
</tr>
<tr>
<td>RV</td>
<td>105%</td>
<td>60%</td>
<td></td>
</tr>
<tr>
<td>FRC</td>
<td>95%</td>
<td>55%</td>
<td></td>
</tr>
<tr>
<td>DICO</td>
<td>50%</td>
<td>50%</td>
<td>&gt;80%</td>
</tr>
</tbody>
</table>

**Six Minute Walk Testing in ILD**

Patient encouraged to walk at a maximal pace with as many stops as necessary.

Oxygenation (desaturation) and symptom scores are measured.

Desaturation may occur in other conditions:
- Pulmonary hypertension
- Severe COPD
- Heart failure

**Six Minute Walk Testing in ILD**

Primary end-point is distance walked.

6MWT distance is used as a primary endpoint in clinical trials for ILD therapy.

Degree of desaturation may have prognostic significance.

**Desaturation during initial 6MWT predicts decreased survival:**

<table>
<thead>
<tr>
<th>Disease</th>
<th>Desaturation</th>
<th>4-Year Survival</th>
</tr>
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<tbody>
<tr>
<td>UIP (IPF)</td>
<td>Yes</td>
<td>35%</td>
</tr>
<tr>
<td>No</td>
<td>69%</td>
<td>n=83, p=0.0018</td>
</tr>
<tr>
<td>NSIP</td>
<td>Yes</td>
<td>66%</td>
</tr>
<tr>
<td>No</td>
<td>100%</td>
<td>n=22, p=0.0089</td>
</tr>
</tbody>
</table>

**ILD: PLAIN CHEST X-RAY**

**ILD: Early HRCT Findings**

Courtesy of David A. Lynch, MD.
ILD: Early HRCT Findings

ILD: Traction Bronchiectasis

ILD: HONEYCOMBING

ILD: Case Presentation

50 year old man with “rapidly progressive IPF” transferred to CUMC 1/03

Pulm Hx: Cigarette smoking @ 1.5 ppd, teens - 45
Pneumonia 2/02, with full recovery

PMH: Gout
OA

Occupation: Mason
Case Presentation: HPI

7/97-12/00: Subtle bibasilar infiltrates
9/02: Persistent cough
   Mild DOE
11/02: Extensive infiltrates, Restrictive PFT's

Case Presentation: HPI

12/02: Surgical Lung Biopsy
   (Lingula & SS-LLL)
12/02: Predisone 60 mg/d (0.7 mg/kg/d)
12/02: URI, oral antibiotics
   Acute decompensation
   Dexamethasone 30 mg/d

Case Presentation: HRCT

CASE PRESENTATION: HRCT

Case Presentation: Clinical Course

3/03: Prednisone 25 mg/d
   Pulmonary Rehabilitation
   Less Dyspneic
4/03: Transplant Evaluation
   PA 25/13 (17)
   PCW (2)
7/03: Off Prednisone
   Full-time work
   SpO2 95 - 83% with stair climbing

Case Presentation: PFT's

<table>
<thead>
<tr>
<th>DATE</th>
<th>1/03</th>
<th>3/03</th>
<th>4/03</th>
<th>7/03</th>
<th>9/03</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVC</td>
<td>2.5L (59%)</td>
<td>2.6</td>
<td>3.0</td>
<td>3.1</td>
<td>2.9</td>
</tr>
<tr>
<td>FEV1</td>
<td>2.2L (63%)</td>
<td>2.3</td>
<td>2.7</td>
<td>2.8</td>
<td>2.7</td>
</tr>
<tr>
<td>F/V</td>
<td>88%</td>
<td>88%</td>
<td>90%</td>
<td>90%</td>
<td>91%</td>
</tr>
<tr>
<td>TLC</td>
<td>3.7L (61%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FRC</td>
<td>2.0L (65%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DLCO</td>
<td>7.8L (24%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>SpO2 (R)</td>
<td>92%</td>
<td>89%</td>
<td>92%</td>
<td>95%</td>
<td>91%</td>
</tr>
<tr>
<td>SpO2 (EX)</td>
<td>81%</td>
<td>79%</td>
<td>83%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6MWT</td>
<td>1365</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tbody>
</table>
Case Presentation: Exercise Physiology

<table>
<thead>
<tr>
<th>CPET</th>
<th>1/8/03</th>
<th>10/7/03</th>
</tr>
</thead>
<tbody>
<tr>
<td>TIME</td>
<td>7 min</td>
<td>8 min</td>
</tr>
<tr>
<td>MAX WORK</td>
<td>65 watts</td>
<td>60 watts (32%)</td>
</tr>
<tr>
<td>VO2-max</td>
<td>12.2 ml/min/kg (37%)</td>
<td>11.1 (34%)</td>
</tr>
<tr>
<td>VE/VCO2</td>
<td>47</td>
<td>51</td>
</tr>
<tr>
<td>MVV</td>
<td>86 L/min (58%)</td>
<td>124 (85%)</td>
</tr>
</tbody>
</table>

Progression of IPF: Acute Exacerbation vs Slow Decline

Pathological Sections Demonstrating UIP

- a. Peripheral accentuation of the disease
- b. Transition into uninvolved lung
- c. Low power pathology
- d. High power image of fibroblastic focus

Myofibroblast Proliferation in UIP

Multiple Hypotheses for the Pathogenesis of IPF

- Inflammation causes fibrosis
- Noninflammatory (multiple hit) hypothesis: fibrosis results from epithelial injury and abnormal wound healing in the absence of chronic inflammation
- Vascular remodeling: aberrant vascular remodeling supports fibrosis, and may contribute to increased shunt and hypoxemia
- Abnormalities in host defense.
Inflammatory Hypothesis

- **Inflammation causes fibrosis**
  - Inflammatory concept was dominant in the 1970s and 1980s
  - IPF resulted from unremitting inflammatory response to injury culminating in progressive fibrosis
  - Role of inflammation remains controversial

Vascular Remodeling Hypothesis

- **Aberrant vascular remodeling supports fibrosis and may contribute to increased shunt and hypoxemia**
  - Increased angiogenesis results from imbalance of pro-angiogenic chemokines (IL-8, ENA-78) and anti-angiogenic, IFN-inducible chemokines (IP-10)
  - Vascular remodeling leads to anastomoses between the systemic/pulmonary microvasculature, increasing right-to-left shunt, contributing to hypoxemia

Defects in Host Defense Mechanisms May Contribute to Fibrosis

- **Defects in endogenous host defense mechanisms (eg, IFN-γ, PGE2 production) that limit fibrosis after acute lung injury may contribute to progressive fibrosis**

Center for Interstitial Lung Disease

A multi-disciplinary group at NY-Presbyterian Hospital, based in the Jo-Ann LeBuhn Center for Chest Disease

Goals:
- Diagnosis
- Monitoring disease progression
- Coordination of therapy
- Clinical trials
- Investigative research

<table>
<thead>
<tr>
<th>Pulmonologists</th>
<th>Clinical coordinators</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung pathologists</td>
<td>Physical therapists</td>
</tr>
<tr>
<td>Chest radiologists</td>
<td>Respiratory techs.</td>
</tr>
<tr>
<td>Exercise Physiologists</td>
<td>Outside consultants</td>
</tr>
<tr>
<td>Rheumatologists</td>
<td>Cardiologists</td>
</tr>
<tr>
<td>Transplant physicians</td>
<td>Thoracic surgeons</td>
</tr>
<tr>
<td>Basic researchers</td>
<td>(Medical Informatics)</td>
</tr>
<tr>
<td><strong>Center for Interstitial Lung Disease</strong></td>
<td></td>
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<tr>
<td>----------------------------------------</td>
<td></td>
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<tr>
<td>Potential system-wide goals &amp; projects:</td>
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<tr>
<td><strong>Data base</strong></td>
<td></td>
</tr>
<tr>
<td>Diagnosis, natural history, pathogenesis</td>
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</tr>
<tr>
<td><strong>Diagnosis</strong></td>
<td></td>
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<tr>
<td>Central review of cases, clinical conferences</td>
<td></td>
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<tr>
<td><strong>Coordination of care</strong></td>
<td></td>
</tr>
<tr>
<td>Clinical trials, transplant/tertiary care</td>
<td></td>
</tr>
<tr>
<td><strong>Basic research</strong></td>
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