Interstitial Lung Diseases:
A Synopsis

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Objectives

1. History, Nomenclature, and Classification of ILD
2. Acute Diseases (hours/days to weeks)
   • DAD (AIP), EP, Vasculitis/DAH, Drug, CVD
3. Subacute Diseases (weeks to months)
   HSP, Sarcoid, NSIP, Drugs, Smoking (RBILD and PLCH), “Chronic” EP, Constrictive bronchiolitis, CVD
4. Chronic Diseases (months to years)
   UIP, Fibrotic NSIP, Pneumoconioses, CVD-related, Chronic HSP, Smoking (RBILD and PLCH), Constrictive bronchiolitis, angiopathic diseases

“ILD” in a Nutshell

Diffuse lung diseases of “known” etiology

- Sarcoidosis/Berylliosis
- Hypersensitivity
- Eosinophilic pneumonia
- RBILD
- Diffuse alveolar damage

- Diseases related to CVD
- Diseases related to drugs
- Pneumoconioses
- Alveolar proteinosis
- Organizing pneumonia
- Amyloidosis
- Lymphangitis
- Vasculitis/DPH

Diffuse lung diseases of “unknown” etiology (idiopathic)

- Usual interstitial pneumonia (UIP)
- Desquamative interstitial pneumonia (DIP)
- Non-specific interstitial pneumonia (NSIP)
- Lymphocytic interstitial pneumonia (LIP)
- Cryptogenic organizing pneumonia (COP)
- Acute interstitial pneumonia (AIP)

- Alveolar proteinosis (PAP)
- Lymphangioleiomyomatosis (LAM)
- Pulmonary hemosiderosis (IPH)
- Small airways disease (SAD)
Autopsy studies had identified “muscular cirrhosis” and “honeycomb lung” disease.

**History**

Liebow Years
(UIP, DIP etc)

Era of better imaging and lung biopsy

- 1900
- 1935
- 1952
- 1964
- 2000

**Liebow’s Classification**

- UIP
- BIP
- DIP
- LIP
- GIP

**European Classification**

- Cryptogenic Organizing Pneumonia (COP)
- Cryptogenic Fibrosing Alveolitis (CFA)

- GIP => cobalt pneumoconiosis
- LIP => Maltoma => HIV related
- BIP => BOOP => COP!
- DIP => DIP/RBILD => smoking

**International Consensus Classification of the Idiopathic Interstitial Pneumonias**

- **Acute**
  - Acute interstitial pneumonia (AIP)
- **Subacute**
  - Nonspecific interstitial pneumonia (P) (NSIP)
  - Cryptogenic Organizing Pneumonia (COP)
  - Desquamative interstitial pneumonia (DIP)
  - Respiratory bronchiolitis-associated interstitial lung disease (RBILD)
  - Lymphoid interstitial pneumonia (LIP)
- **Chronic**
  - Usual interstitial pneumonia (UIP)
## Clinical Disease Onset

<table>
<thead>
<tr>
<th>Acute Diseases</th>
<th>Subacute Diseases</th>
<th>Chronic Diseases</th>
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<tbody>
<tr>
<td>Hours to Days</td>
<td>Weeks to Months</td>
<td>Months to Years</td>
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<tr>
<td>Diffuse alveolar damage (shock/infection)</td>
<td>Organizing pneumonia</td>
<td>Pneumococcioses</td>
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<tr>
<td>Acute eosinophilic pneumonia</td>
<td>Hyperreactivity</td>
<td>Lymphangitic tumor</td>
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<td>Diseases related to drugs and toxins</td>
<td>RBILD/DIP/PLCH</td>
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<td>Sarcoidosis/Berylliosis</td>
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<td>Acute exacerbation of IPF</td>
<td>Chronic eosinophilic pneumonia</td>
<td>Small airways disease</td>
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<tr>
<td></td>
<td>NSIP</td>
<td>Amyloidosis</td>
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<td>LIP</td>
<td>LAM</td>
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<td>UIP</td>
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</table>

### II. Diffuse Lung Diseases with Acute Manifestations

- Acute lung injury/Diffuse alveolar damage
- Acute eosinophilic pneumonia
- Vasculitic diseases

### DIFFUSE ALVEOLAR DAMAGE

- [Image of lung CT scan]
I. Diffuse Lung Diseases with Acute Manifestations

- Immunologic Diseases
- Trauma/Shock
- DAD
  - Idiopathic
- Infection/Sepsis
- Toxins

II. Diffuse Lung Diseases with Acute Manifestations
Phases of ARDS

- Exudative
- "Transition"
- Proliferative
- Fibrotic

Edema
Inflammation
Hyaline membranes
Fibroplasia

Day 0
Day 1
Day 2
Day 3
Day 4
Day 5
Day 6
Day 7
Later

% of Maximal Prominence

- Day 0
- Day 1
- Day 2
- Day 3
- Day 4
- Day 5
- Day 6
- Day 7
- Later
Phases of ARDS

Exudative → Transition → Proliferative → Fibrotic

%) of Maximal

Day 0 Day 1 Day 2 Day 3 Day 4 Day 5 Day 6 Day 7 Later

Fibrotic
Inflammation
Edema
Hyaline Membranes
Fibroplasia

Transition
II. Diffuse Lung Diseases with Acute Manifestations

DAD with Hyaline Membranes
Infection Drug reactions Collagen vascular disorders
Idiopathic (AIP)

DAD with Necrosis and/or atypical cells w/inclusions
Infection, Infection, Infection
II. Diffuse Lung Diseases with Acute Manifestations

DAD with Eosinophils
Acute Eosinophilic Pneumonia

DAD with Hemosiderin-filled macrophages
Look for capillaritis/necrotizing vasculitis
Hemorrhage syndromes Drugs Collagen vascular disorders

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<td>Acute eosinophilic pneumonia, Diseases related to drugs and toxins, Vascularitis/DPH, AIP</td>
<td>Diseases related to drugs, Chronic eosinophilic pneumonia, NSIP, LIP</td>
<td>Lymphangitic tumor, RBILD/DIP/PLCH, Sarcoidosis/Berylliosis, Alveolar proteinosis, Constrictive bronchiolitis, Amyloidosis, LAM, UIP</td>
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</tbody>
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III. Diffuse Lung Diseases with Subacute Manifestations

Hypersensitivity Pneumonitis
- From inhaled antigens
- From drugs

Low grade infection
- Atypical mycobacteria

Connective tissue diseases
- SLE
- MCTD
- RA
- Sjogren
- Scleroderma
- Dermatomyositis/polymyositis
- Chronic eosinophilic pneumonia

Idiopathic NSIP

Non-Specific Interstitial Pneumonia (NSIP)

“A fairly sizeable group of idiopathic interstitial pneumonias cannot be pigeonholed into one of the three main groups [of Liebow]”

Katzenstein

NSIP
“NSIP”

Single episode of injury

Cellular interstitial pneumonia

+/-

Uniform interstitial fibrosis

Cellular NSIP

Fibrotic NSIP
Different Patterns of Fibrosis

- NSIP/F
- UIP

Subtypes of NSIP vs UIP

<table>
<thead>
<tr>
<th>Survey years</th>
<th>Cellular NSIP</th>
<th>NSIP</th>
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Additional Diffuse Lung Diseases with Subacute Manifestations

- With Lymphocytes and plasma cells +/- poorly-formed granulomas

- Hypersensitivity pneumonitis
- Non-specific interstitial pneumonia
- Low grade lymphoma

- Certain drug reactions
- Resolving phase of some infections or acute lung injury
Hypersensitivity Pneumonitis

- With well-formed Granulomas
- Infections (AFB and fungus)
- Sarcoidosis/berylliosis
- Aspiration

Additional Diffuse Lung Diseases with Subacute Manifestations

- With well-formed Granulomas
  - Infections (AFB and fungus)
  - Aspiration
  - Sarcoidosis/berylliosis
Additional Diffuse Lung Diseases with Subacute Manifestations
- With organizing pneumonia pattern
  - Organizing infection
  - Reaction to drug or toxin
  - Collagen vascular diseases
  - Idiopathic (COP)

Additional Diffuse Lung Diseases with Subacute Manifestations

IV. Diffuse Lung Diseases with Chronic Manifestations
- Fibrotic NSIP
- Connective tissue diseases
  - SLE
  - MCTD
  - RA
  - Scleroderma
  - Sjogren
  - Dermatomyositis

- Pneumoconioses
- Chronic HSP
- Selected drug-related diseases
- Selected airway diseases
- Selected smoking-related disorders

UIP

ATS/ERS Consensus Statement on IPF
ATS/ERS, Am J Respir Crit Care Med, 2000;161:646.

UIP is a histologic lesion that can only be recognized by surgical (wedge) lung biopsy.

Surgical lung biopsy recommended in patients with suspected IPF, especially those with atypical clinical or radiologic features.

Transbronchial lung biopsy is limited to the exclusion of other conditions.
IPF Overview


• **Prevalence:** 13–20/100,000 in US
  (approximately 35,000-55,000 cases)
• **Onset:** Typically between 50 and 70 yrs
• **Clinical presentation:**
  • Progressive dyspnea on exertion (months to years)
  • Paroxysmal cough, usually nonproductive
  • Abnormal breath sounds on chest auscultation
  • Abnormal chest x-ray or HRCT
  • Restrictive pulmonary physiology with reduced lung volumes and Dlco, and widened AaPO2

Pathogenesis and Course of UIP


Recurrent microscopic injury, occurring over many years

Focal fibroblast proliferation (fibroblastic foci)

Sudden

Death

Respiratory

Death

Collagen deposition

Recurrent microscopic injury

Collagen deposition

Recurrent microscopic injury

HRCT Findings in Late IPF
Honeycomb lung

Early HRCT Findings in IPF

HRCT Findings NOT Typical of IPF

"NSIP"
"LIP" in Sjögren's Syndrome
Mainly upper lobe disease
Pathology of UIP/IPF

“Oldest” disease (fibrosis) is peripheral in the lung lobule or acinus (with variable microscopic honeycombing)

Pathology of UIP/IPF

Transition to uninvolved lung present in the biopsy
Pathology of UIP/IPF
Leading edge of “fibroblastic foci”.

Pathology of UIP/IPF
Microscopic Honeycombing

UIP Survival
(from Bjoraker al et)
Step theory of UIP/IPF progression

Recurrent clinical episodes of deterioration

Acute Exacerbation

Years
1 2 3 4

Respiratory function/symptoms

Smoking-related ILDs

Respiratory bronchiolitis ILD
Desquamative interstitial pneumonitis
Pulmonary Langerhans cell histiocytosis
Idiopathic pulmonary fibrosis, including UIP and CPFE

Note.—CPFE = combined pulmonary fibrosis with emphysema, UIP = usual interstitial pneumonia.
Combined Pulmonary Fibrosis and Emphysema

The combination of emphysema in the upper lobes and fibrosis in the lower lobes (CPFE) is being increasingly recognized as a distinct entity in smokers.

Patients are almost exclusively men in their 6th and 7th decades.

Lung volumes are relatively preserved despite markedly impaired diffusion capacity and hypoxemia during exercise.

Honeycombing, reticular opacities, and traction bronchiectasis are the most frequent findings at high-resolution CT in the lower lungs, while the upper lungs exhibit paraseptal and centrilobular emphysema.
Chronic Interstitial Lung Disease—Pneumoconioses

Defined partly by their patterns of interstitial fibrosis, but principally by detection and quantitation of the inhaled foreign materials that cause them—

- Anthracosilicosis—Silica & carbon
- Asbestosis—Asbestos
- Bauxite fibrosis—Bauxite
- Berylliosis—Beryllium
- Byssinosis—Cotton
- Stannosis—Tin oxide
(Anthraco-) Silicosis

Asbestosis
Prognostic Classification of ILD

Leslie’s Histopathology Color Index Diffuse Lung Diseases