Usual Interstitial Pneumonia (UIP)

Histologic features of UIP

Key Histologic Features

- Dense fibrosis causing remodeling of lung architecture with frequent "honeycomb" fibrosis
- Fibroblastic foci typically scattered at the edges of the dense scars
- (TEMPORAL HETEROGENEITY)
- Patchy lung involvement
- Frequent subpleural, paraseptal and/or bronchovascular distribution

Pertinent Negative Findings

- Lack of active lesions of other interstitial diseases (i.e. sarcoidosis or Langerhans cell histiocytosis)
- Lack of marked interstitial chronic inflammation
- Granulomas: inconspicuous or absent
- Lack of substantial inorganic dust deposits, i.e., asbestos bodies (except for carbon black pigment)
- Lack of marked eosinophilia

MINOR HISTOPATHOLOGICAL FEATURES IN USUAL INTERSTITIAL PNEUMONIA

- Dense scar
- Micro Honeycombing
- Fibroblast focus

THIS IS UIP
Revised ATS/ERS IIP Classification
(to be viewed as a supplement to the 2002 document)
Am J Respir Crit Care Med 2013; 188: 733-748

Clinical Radiologic Pathologic Diagnosis
- Idiopathic Pulmonary Fibrosis
- Idiopathic Nonspecific Interstitial Pneumonia
- Respiratory Bronchiolitis Interstitial Lung Disease
- Desquamative Interstitial Pneumonia
- Cryptogenic Organizing Pneumonia
- Acute Interstitial Pneumonia

Rare IIP
- Idiopathic LIP
- Idiopathic pleuroparenchymal fibroelastosis

Rare Histologic Patterns
- Acute fibrinous & organizing pneumonia
- Bronchiolocentric patterns of IP

Unclassifiable IIP

CO-EXISTING PATTERNS IN IPs
PLEUROPARENCHYMAL FIBROELASTOSIS AND UIP

Histologic pattern of UIP in non-IPF patients.
- Most are seen in the context of IPF but...
- Chronic Hypersensitivity Pneumonitis (EAA)
- Collagen Vascular Disease (RA, PM, SS)
- Asbestosis
- Familial Idiopathic Pulmonary Fibrosis
- Drug Toxicity (Usually cytotoxic drugs)

UIP and chronic HP
- Pathologic patterns and survival in Chronic HP.
- Chung et al. AJSF 2009;33:1765
- 24 subacute (cellular, nonfibrotic) and 25 chronic (fibrotic) HP.
- 72% chronic HP = UIP-like;
  three BIPF;
- 16% F-NSIP
- Only 2 UIP-like cases could not be morphologically distinguished from idiopathic UIP.
- Survival for patients with no fibrosis = 22.4 years
- Fibrotic NSIP = 2.1 years;
- UIP-like pattern = 2.8 years
**Chronic HP versus UIP/IPF....**

**BUILD 1 drug trial**

<table>
<thead>
<tr>
<th>Patient subset</th>
<th>All patients</th>
<th>Placebo</th>
<th>Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnosis of IPF/UIP (local panel)</td>
<td>100</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>All cases reviewed by the local pathology panel</td>
<td>98</td>
<td>49</td>
<td>49</td>
</tr>
<tr>
<td>Cases confirmed by outside pathology panel</td>
<td>94</td>
<td>47</td>
<td>47</td>
</tr>
</tbody>
</table>

25% of cases rejected as not UIP by reference pathologists

23% EAA (8% in total)

**Histopathologic pattern and clinical features of rheumatoid arthritis-associated interstitial lung disease**

- UIP – 13, NSIP – 6, and alveolar disease - 2.
- In three patients, EG/psoriasiform, 2 simultaneous diagnosis

**Interstitial pneumonia in RA**

- Pulmonary fibrosis seen in about 3-4% of patients
- NSIP and follicular bronchiolitis are common among histologic patterns, often superimposed in Bronchiolitis obliterans.
- Early studies suggest survival similar to idiopathic NSIP

**UIP AND ASBESTOSIS**


- Interstitial fibrosis and asbestos bodies 2-10mm per cm² in a normal thickness section.
- Interstitial fibrosis of asbestosis is accompanied by very little inflammation, although not marked, in better developed, idiopathic pulmonary fibrosis.
- In keeping with the slow tempo of the disease, the histologic features are characteristic of idiopathic pulmonary fibrosis.
- Asbestos is almost always accompanied by renal fibrosis of the visceral pleura, a feature that is rare in idiopathic pulmonary fibrosis.

**UIP AND ASBESTOSIS**


- Asbestos exposure associated with UIP.
- Asbestos cutaneous or ocular diseases.
- The incidence of idiopathic pulmonary fibrosis (IPF) in the population.
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- F-IIP: unexplained occurrence of diffuse parenchymal lung disease in related individuals, said to be indistinguishable from UIP/IPF.
- 30 patients - consensus diagnosis was “unclassifiable” parenchymal fibrosis (60%), with a high incidence of histopathologic honeycombing, fibroblast foci, and smooth muscle in fibrosis.
- UIP, strictly defined, was identified in less than half of the F-IIP cases (range, 23%-90%), interobserver agreement was fair (κ = 0.37).
- Subjects with UIP had a shorter survival and younger age at death.

**Drug reactions – May not be the systemic disease but its treatment that causes pulmonary pathology**

- Very rarely is a histologic pattern specific for a drug reaction (eg amiodarone)
- May however be pointers
  - A1. Eosinophilia
  - A2. Cytologic atypia within epithelial cells
  - A3. UIP pattern is rare

**www.pneumotox.com**
**Conclusion: Histologic pattern of UIP in non-IPF patients.**

- Most are seen in the context of IPF but...
- Chronic Hypersensitivity Pneumonia (HP)
- Collagen Vascular Diseases (RA, PM, SSc)
- Drug Toxicity (Usually cytotoxic drugs)
- Asbestosis
- Familial Idiopathic Pulmonary Fibrosis

If a pattern of UIP is made on histology, look for features that argue against a diagnosis of IPF and comment, if present.

- Granulomas, bronchocentricity, areas of inflammation without fibrosis, areas of organizing pneumonia, asbestosis bodies, pathology in other anatomic compartments (pleura, vasculature, airways), prominent eosinophils

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**Non-specific Interstitial Pneumonia (NSIP)**

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**ATS/ERS consensus classification of idiopathic interstitial pneumonias**

*Am J Respir Crit Care Med 2002; 165: 266-301*

<table>
<thead>
<tr>
<th>HISTOLOGIC PATTERN</th>
<th>CLINICOPATHOLOGIC DIAGNOSIS</th>
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<tbody>
<tr>
<td>Usual interstitial pneumonia</td>
<td>Idiopathic Pulmonary Fibrosis</td>
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<tr>
<td>Non-specific interstitial pneumonia</td>
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</tr>
<tr>
<td>Respiratory Bronchiolitis (RB)</td>
<td>RB-associated ILD (RB-ILD)</td>
</tr>
<tr>
<td>Desquamative interstitial pneumonia</td>
<td>Desquamative ILD (RB ILD)</td>
</tr>
<tr>
<td>Diffuse alveolar damage</td>
<td>Acute interstitial pneumonia</td>
</tr>
<tr>
<td>Organising pneumonia</td>
<td>Cryptogenic organising pneumonia</td>
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<tr>
<td>Lymphoid interstitial pneumonia</td>
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**ATS/ERS subdivision of NSIP**

- Cellular
- Fibrotic

ATS/ERS workshop: AJRCCM 2008;177:1388-47

- Sixty-seven cases (out of 305)
- Mean age was 52 years, 67% were women, 69% were never smokers
- Dyspnea (96%) and cough (87%); 69% had restriction
- HRCT: lower lung predominant, reticular pattern (87%) with traction bronchiectasis (82%) and volume loss (77%)
- Five-year survival was 82.3%

- Distinct clinical entity that occurs mostly in middle-aged women who are never-smokers. The prognosis of NSIP is very good.
58, male
- Two years of exertional dyspnoea
- No obvious steroid effect on disease course
- Bilateral basal crackles, not clubbed
- Life-long non-smoker
- No CTD symptoms
- No occupational exposures
- BAL: normal differential
- Restrictive PFT, FVC 61%, DLco 57%

UIP, consistent with IPF
Histopathology: F-NSIP

- MDT review:
  - HRCT favours chr HP
  - History of bird exposure
- Levels cut on blocké

**FINAL DIAGNOSIS:**
- CHR HP

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**Update on NSIP…**

- **SOME PATIENTS WITH IDIOPATHIC NSIP SUBSEQUENTLY DEVELOP COLLAGEN VASCULAR DISEASES**
  - 17% developed CVD during the follow-up period (5.5 ± 5.0 years);
  - (DM = 3, DM/Sjogren’s syndrome = 2, RA = 1)
- **SUBDIVISION OF PATIENTS WITH A BIOPSY SHOWING NSIP PROVIDES PROGNOSTIC INFORMATION**
  - Nunes H. Nonspecific interstitial pneumonia: survival is influenced by the underlying cause. Eur Respir J. 2015;45:746-55.
- Survival was better for UCTD than for idiopathic NSIP.
- cHP survival tended to be poorer than that of idiopathic NSIP (p=0.087) and was an independent predictor of mortality.
- **INTERSTITIAL PNEUMONIA WITH AUTOIMMUNE FEATURES (IPAF) – A NEW ENTITY**
  - A designation of IPAF should be used to identify individuals with IIP and features suggestive of, but not definitive for, a CTD.

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<td>++</td>
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<tr>
<td>NSIP</td>
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The prevalence of patterns exists in CTDs as for idiopathic disease.

- The prevalence differs overall (NSIP common).
- The prevalence of IP patterns differs for each CTD.
- Treatment and progresses differ from idiopathic disease.

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<td>LIP/FB</td>
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<tr>
<td>OP</td>
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<tr>
<td>DAD</td>
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<tr>
<td>DIP/RB</td>
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The prevalence of patterns exists in CTDs as for idiopathic disease.

- The prevalence differs overall (NSIP common).
- The prevalence of IP patterns differs for each CTD.
- Treatment and progresses differ from idiopathic disease.
Disease overlap in Interstitial Lung Disease

Other anatomic compartments...

Diffuse lung disease in infancy and childhood: expanding the chILD classification (0-2 years/2-18 years/mimics of ILD).

2 year old female

Increasing shortness of breath, ?ILD

c.218T>C in the SFTPC gene
Non-specific interstitial pneumonia in children

2003

2013

Bronchoscopic cryobiopsy in NSIP diagnosis

B. Cryobiopsies have a higher diagnostic yield than transbronchial biopsies. (6)
C. Similar complication rate (2). (6)
D. Bronchoscopic cryobiopsy has a meaningful impact on diagnostic confidence in NSIP. (6)
E. Costs efficiency (the systematic use of cryobiopsy avoids up to 100% of additional biopsies performed in the first year and £478 in subsequent years). (6)

Rate of NSIP in cryobiopsies....

<table>
<thead>
<tr>
<th>Study</th>
<th>Rate NSIP</th>
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<tbody>
<tr>
<td>A</td>
<td>16/20</td>
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<tr>
<td>B</td>
<td>15/20</td>
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<tr>
<td>C</td>
<td>11/15</td>
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<tr>
<td>D</td>
<td>5/5</td>
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<tr>
<td>E</td>
<td>3/3</td>
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12 month old female
Born three weeks prematurely (birth weight 3.5kg) with severe hyaline membrane disease that required ventilation for 10 days. Has since had recurrent respiratory tract infections
UIP, NSIP and their differential diagnoses

**ATS/ERS Revised 2013 Classification**

- **Clin-Rad**
  - Idiopathic Pulmonary Fibrosis
  - Idiopathic Nonspecific Interstitial Pneumonia
  - Respiratory Bronchiolitis
  - Interstitial Lung Disease
  - Desquamative Interstitial Pneumonia
  - Cryptogenic Organizing Pneumonia
  - Acute Interstitial Pneumonia

- **Histologic Patterns**
  - Rare IIPs
    - Lymphoid Interstitial Pneumonia
    - Langerhans Cell Histiocytosis
  - Unclassifiable IIP

**UIP and NSIP**

- UIP and overlapping histology on cryobiopsy

**Size and Number of Biopsy Sites and Number of Biopsies**

- Lower lobe: UIP
- Middle lobe: NSIP

**Size and Number of Biopsy Sites and Number of Biopsies**

- Lower lobe: UIP
- Upper lobe: NSIP

**UIP is the prognostic indicator**


**UIP, NSIP and their differential diagnoses**

- UIP, NSIP and their differential diagnoses
- UIP and overlapping histology on cryobiopsy
- Need identical MDT review as for SLBx, possibly even more important.