Interstitial Lung Disease: An Overview

Justin Oldham, MD MS
Assistant Professor of Medicine
Director, Interstitial Lung Disease Program
University of California at Davis

UC DAVIS
UNIVERSITY OF CALIFORNIA

Disclosures

- Grants to study Genomic Predictors of IPF Outcomes
  - National Institutes of Health (NHLBI)
  - American Thoracic Society
  - American Lung Association

- Grant to study early ILD detection
  - UC-Davis Gordon Wong endowment

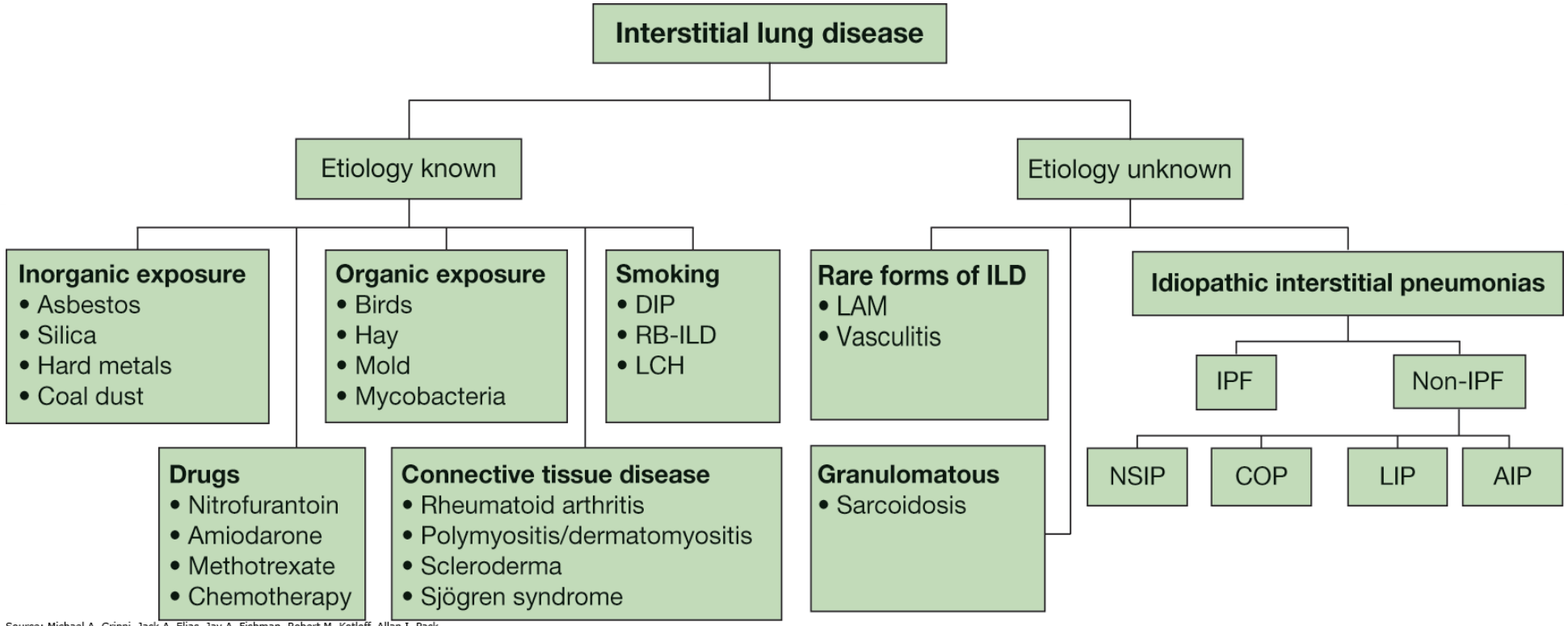
- IPF Consulting
  - Genentech
  - Boehringer Ingelheim

UCDAVIS

Objectives

- Understand the classification framework for common interstitial lung diseases (ILD)
- Appreciate the wide spectrum of ILD presentation
- Pursue a standardized ILD diagnostic work-up

What the textbook says: Interstitial Lung Disease Classification



Source: Michael A. Grippi, Jack A. Elias, Jay A. Fishman, Robert M. Kotloff, Allan I. Pack, Robert M. Senior, Mark D. Siegel: *Fishman's Pulmonary Diseases and Disorders*: www.accessmedicine.com

UCDAVIS

Grippi et al. Fishman's Pulmonary Diseases and Disorders

What we actually see on a regular basis

Interstitial Lung Disease

Etiology Known

Connective tissue disease
- RA, SSc, Sjogrens, IIM

Environmental ILD
- Hypersensitivity pneumonitis

Occupational ILD
- Asbestosis/Silicosis

Drug-induced ILD
- Amio/MTX/Chemo

Idiopathic Interstitial Pneumonia

Smoking-related
- Desquamative interstitial pneumonia
- Respiratory bronchiolitis-ILD

Chronic Fibrosing
- Idiopathic pulmonary fibrosis
- Idiopathic NSIP

Inflammatory +/- fibrosing
- Cryptogenic organizing pneumonia

Unclassifiable

None of the above

Other
- Sarcoidosis

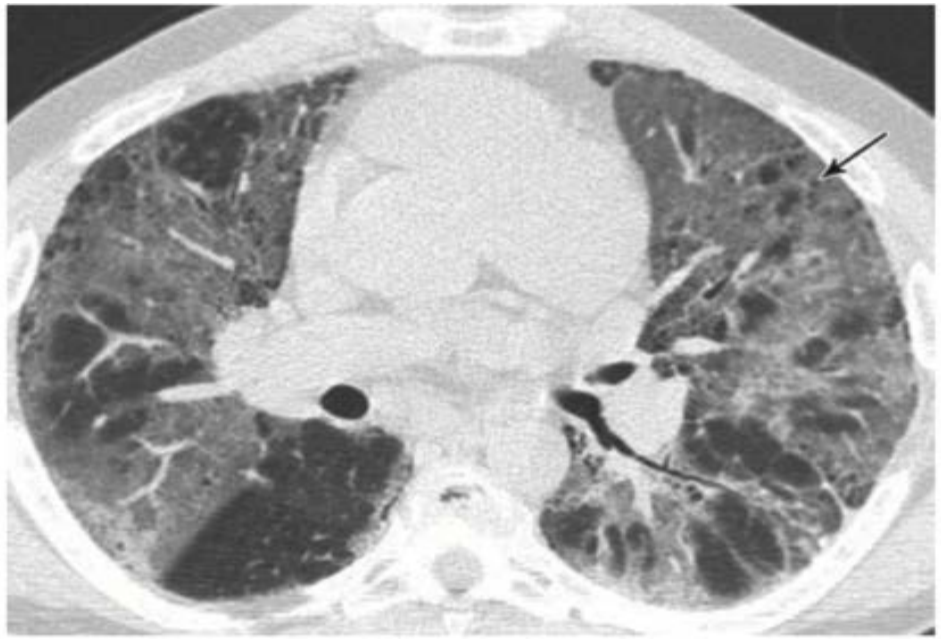
UCDAVIS

Interstitial Lung Disease

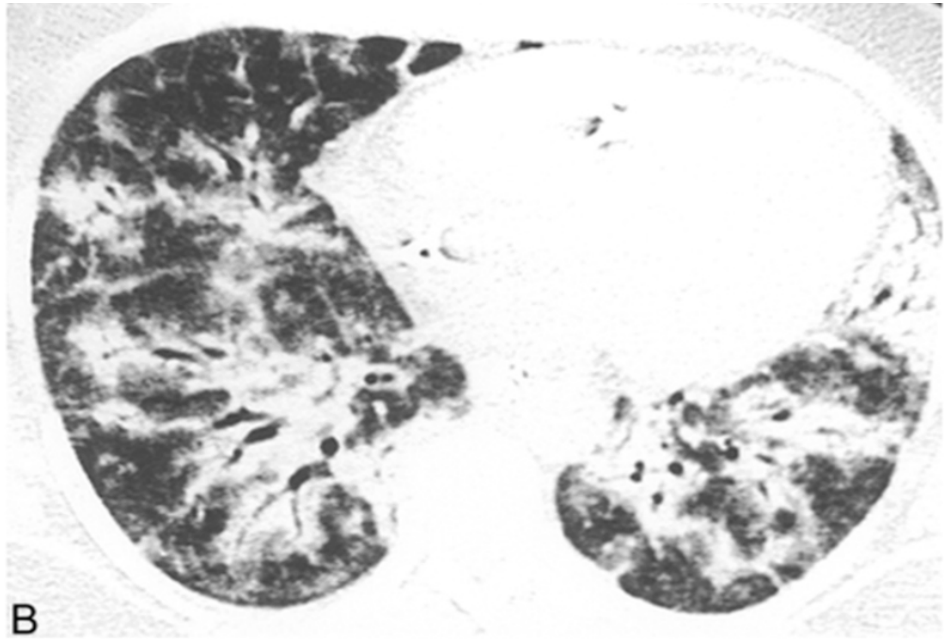
<u>Inflammatory Predominant ILDs</u>
CTD-ILD (most)
Hypersensitivity Pneumonitis (early)
Cryptogenic Organizing Pneumonia
Cellular idiopathic NSIP
Drug-induced ILD

<u>Fibrotic Predominant ILDs</u>
Systemic sclerosis-ILD
Hypersensitivity pneumonitis (late)
Idiopathic pulmonary fibrosis
Fibrotic idiopathic NSIP
Asbestosis

Inflammatory ILD can manifestations as:



Non-specific Interstitial Pneumonia



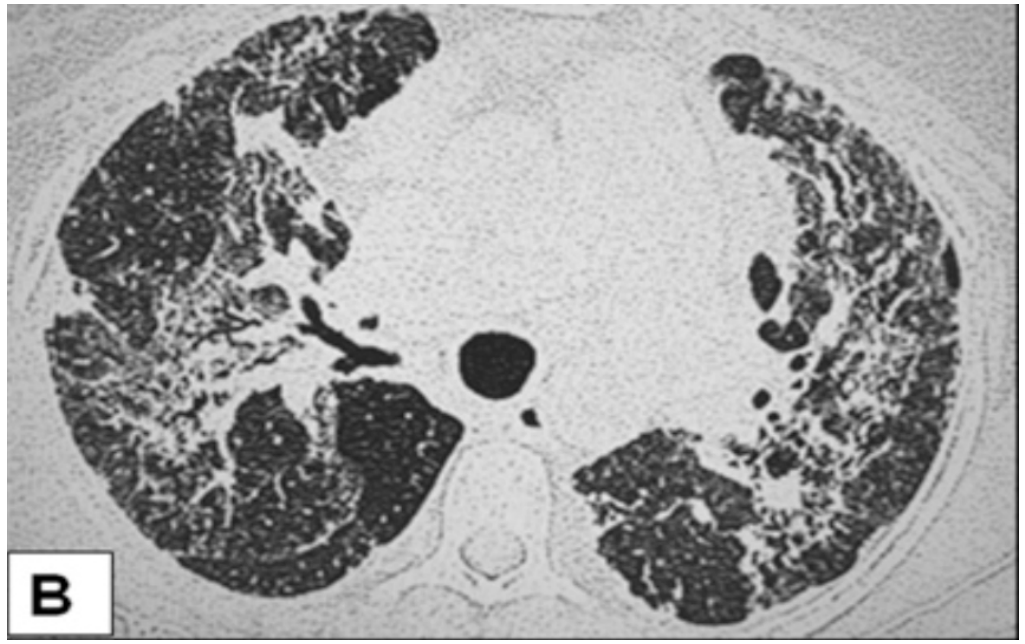
Organizing Pneumonia

UCDAVIS

Kligerman et al.Radiographics 2009
Travis et al. AJRCCM 2013

Fibrotic ILD can manifest as:

Peripheral predominant fibrosis

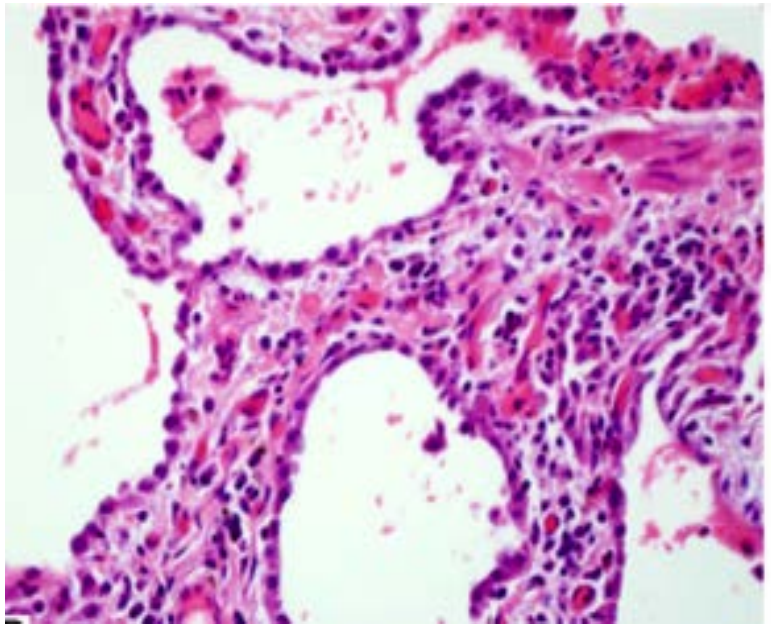


Airway-centric fibrosis

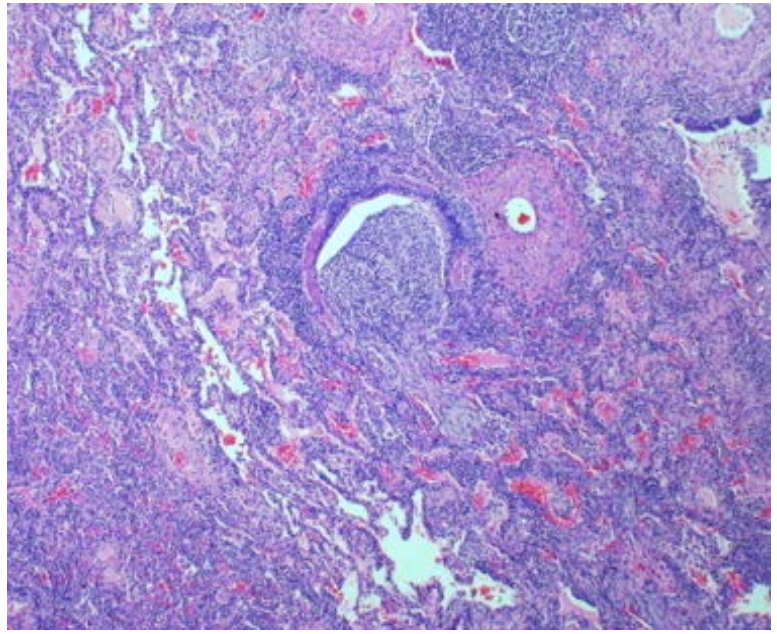
UCDAVIS

Oldham et al. Res Med 2014
Selman et al. AJRCCM 2012

Inflammatory ILD can manifestations as:



Cellular non-specific Interstitial Pneumonia

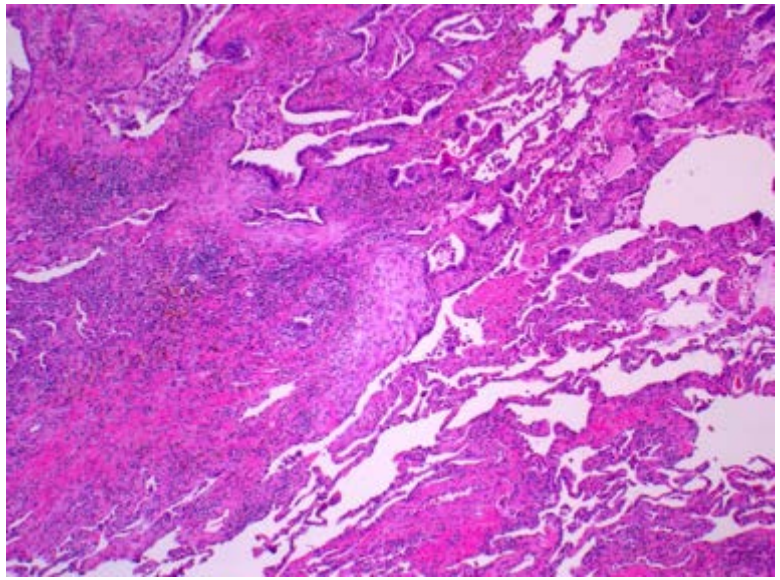


Organizing Pneumonia

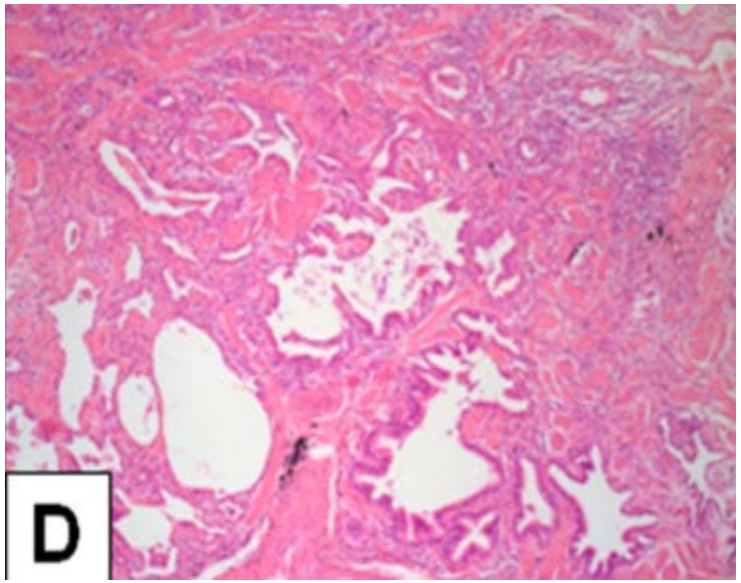
UCDAVIS

Travis et al. AJRCCM 2013

Fibrotic ILD can manifest as:



Usual Interstitial Pneumonia



Airway-centric fibrosis

UCDAVIS

Oldham et al. Res Med 2014
Selman et al. AJRCCM 2012

The ILD Evaluation

Goals

- Standardized work-up to improve diagnostic accuracy
- Avoid unnecessary lung biopsy
- Diagnose early in the disease course
- Treat the disease early

The ILD Evaluation

Laboratory work-up
- Autoimmune serologies

Physical Exam
- Autoimmune features?
- Crackles? Location?

High-resolution CT Scan

History
- Environmental history (Birds, mold)? - HP
- Joint pain/swelling, rash, muscle weakness, skin tightening, dysphagia? - CTD-ILD
- New medication? - Chemo/Amio/MTX
- Job exposures? - asbestosis, silicosis
- Family history of ILD? – familial IPF
- Smoking history? – smoking-ILDs
- Early graying, bone marrow abnormality, liver disease? – short telomere-related ILD

UCDAVIS

The ILD Evaluation

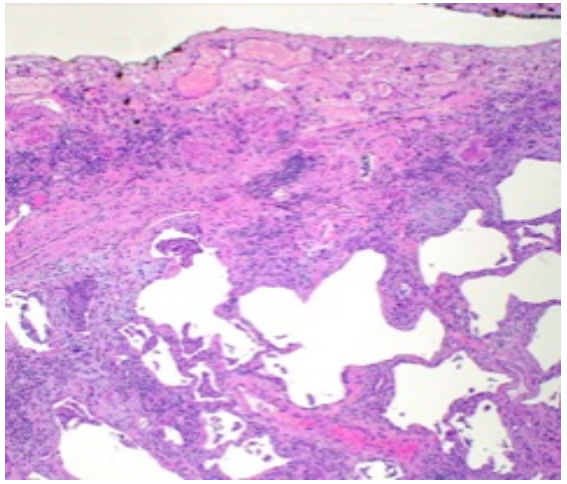
↓

History unrevealing
Physical exam non-specific
Laboratory work-up negative
High-resolution CT non-diagnostic

↓

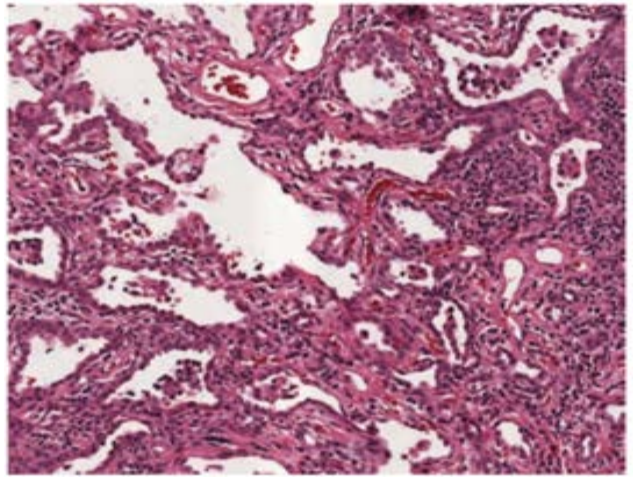
Unclassifiable ILD

↓



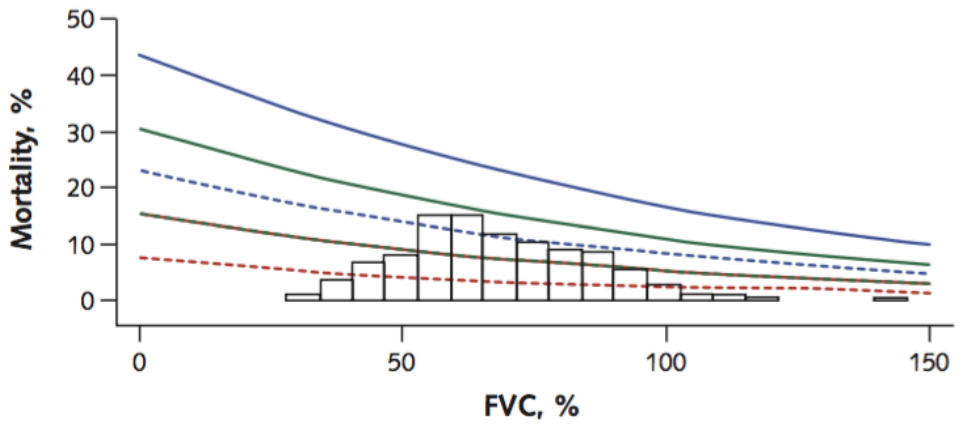
Surgical Lung Biopsy

- **Must have sufficient lung function**
- **Largely safe, but small and finite risk of death and exacerbation**

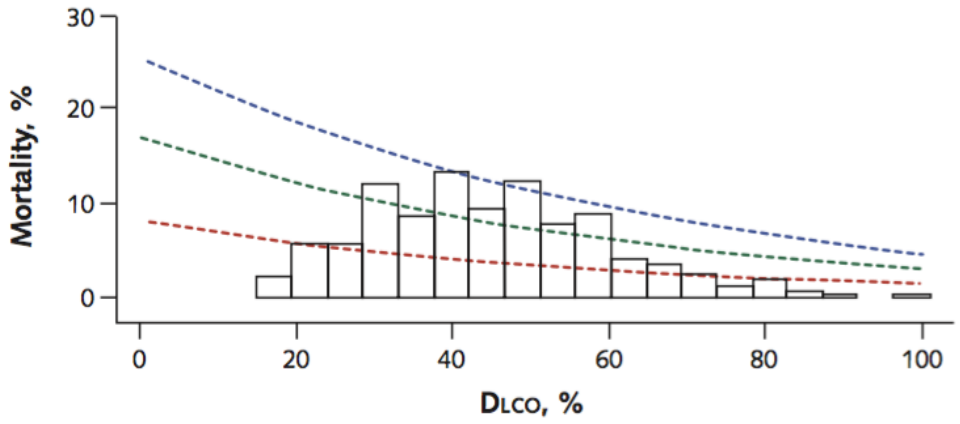


The ILD Evaluation - PFT

- Helps characterize physiology
  - Forced vital capacity (FVC)
  - Diffusion capacity (DLCO)



- Can assist with prognostication
  - Baseline values
  - Longitudinal change over time



UCDAVIS

Ley et al. Ann Int Med 2012

The ILD Evaluation - Bronchoscopy

- Generally of limited use with a few notable exceptions
  - Hypersensitivity pneumonitis – cellular analysis
  - Sarcoidosis – lymph node bx/Tbbx
  - Asbestosis – cellular analysis, histology
  - Amiodarone toxicity – cellular analysis, histology

- Cryobiopsy – larger biopsy performed
  - May establish diagnosis in patients unable to undergo surgical lung biopsy
  - Increased risk of bleeding and pneumothorax
  - Highly operator dependent

The ILD Evaluation – Multi-disciplinary Discussion

Multidisciplinary Approach

The process of achieving a multidisciplinary diagnosis in a patient with IIP is dynamic, requiring close communication between clinician, radiologist, and when appropriate, pathologist (1). Clinical data (presentation, exposures, smoking status, associated diseases, lung function, laboratory findings) and radiologic findings are essential for multidisciplinary diagnosis.

MDD

Pulmonologist

Chest Radiologist

Pulmonary pathologist

UCDAVIS

Travis et al. AJRCCM 2013

How important is a MDD?

Idiopathic Interstitial Pneumonia

What Is the Effe is?

Kevin R. Flaherty, Talm olby,
William D. Travis, Barry ray,
Vibha N. Lama, Steven

Division of Pulmonary and Cr stem, and Department of
Biostatistics, University of Mic ncisco, San Francisco,
California; University of Wash itute of Pathology,
Washington, DC

Figure 1.

Information Provided	Participants	Output
Step 1 - Individual HRCT	Clinicians Radiologists	Diagnosis
Step 2 - Individual HRCT + Standardized clinical data	Clinicians Radiologists	Diagnosis
Step 3 - Group Discussion HRCT + Standardized clinical data	Clinicians Radiologists	Diagnosis
Step 4 - Group Discussion HRCT + Standardized clinical data + SLB	Clinicians Radiologists Pathologists	Diagnosis
Step 5 - Group Discussion HRCT + Standardized clinical data + SLB	Clinicians Radiologists Pathologists	Consensus Diagnosis

UCDAVIS

Flaherty et al. AJRCCM 2004.

How important is a MDE?

Idiopathic Interstitial Pneumonia

What Is the Effect of a Multidisciplinary Approach to Diagnosis?

Kevin R. Flaherty, Talmadge E. King, Jr., Ganesh Raghu, Joseph P. Lynch III, Thomas V. Colby, William D. Travis, Barry H. Gross, Ella A. Kazerooni, Galen B. Toews, Qi Long, Susan Murray, Vibha N. Lama, Steven E. Gay, and Fernando J. Martinez

Division of Pulmonary and Critical Care Medicine and Department of Radiology, University of Michigan Health System, and Department of Biostatistics, University of Michigan School of Public Health, Ann Arbor, Michigan; University of California, San Francisco, San Francisco, California; University of Washington, Seattle, Washington; Mayo Clinic, Scottsdale, Arizona; and Armed Forces Institute of Pathology, Washington, DC

TABLE 3. INTEROBSERVER AGREEMENT AT EACH DIAGNOSTIC STEP

Step	Clinicians [κ (*95% CI*)]	Radiologists [κ (*95% CI*)]	Clinicians–Radiologists [κ (*95% CI*)]	All Observers [κ (*95% CI*)]
1	0.41 (0.29, 0.52)	0.72 (0.57, 0.86)	0.39 (0.29, 0.49)	NA
2	0.51 (0.37, 0.64)	0.80 (0.67, 0.93)	0.44 (0.34, 0.54)	NA
3	0.67 (0.54, 0.79)	0.78 (0.65, 0.91)	0.55 (0.44, 0.66)	NA
4	0.75 (0.64, 0.86)	0.84 (0.72, 0.96)	0.78 (0.70, 0.86)	0.79 (0.71, 0.86)
5	0.86 (0.76, 0.95)	0.90 (0.80, 0.99)	0.88 (0.81, 0.96)	0.88 (0.81, 0.94)

Definition of abbreviations: CI = confidence interval for corresponding statistic; NA = not applicable.

Kappa Score

0.8-1.0 – Excellent
0.6-0.8 – Good
0.4-0.6 – Moderate
0.2-0.4 – Fair
0-0.2 - Poor

UCDAVIS

Flaherty et al. AJRCCM 2004.

ILD General Management Considerations

- Standardized Evaluation
- Multi-disciplinary discussion
- Co-morbidity assessment and treatment
- Pulmonary Rehab referral
- Assessment for supplemental oxygen needs
- Therapeutics
- Clinical Trials

Consider ILD center referral for all patients with ILD

Delayed Access and Survival in Idiopathic Pulmonary Fibrosis

A Cohort Study

Daniela J. Lamas[1], Steven M. Kawut[2–4], Emilia Bagiella[5], Nisha Philip[1], Selim M. Arcasoy[1], and David J. Lederer[1]

[1]Department of Medicine, College of Physicians and Surgeons, Columbia University, New York, New York; [2]Penn Cardiovascular Institute, [3]Department of Medicine, and [4]Center for Clinical Epidemiology and Biostatistics, University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania; and [5]Department of Biostatistics, Mailman School of Public Health, Columbia University, New York, New York

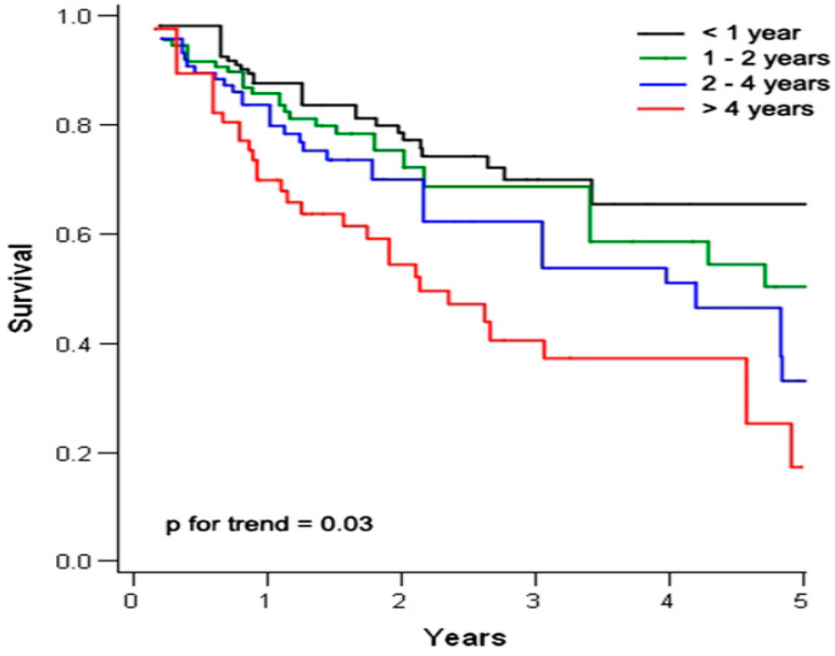


Figure 2. Survival from the time of evaluation at a tertiary care center adjusted for age and FVC across quartiles of delay. Entry time into the cohort began at study enrollment.

UCDAVIS

Lamas et al. AJRCCM 2011

References

- Kligerman SJ, Groshong S, Brown KK, Lynch DA. Nonspecific interstitial pneumonia: Radiologic, clinical, and pathologic considerations. *Radiographics* 2009;29:73-87.

- Travis WD, Costabel U, Hansell DM, King TE, Jr., Lynch DA, Nicholson AG, Ryerson CJ, Ryu JH, Selman M, Wells AU, Behr J, Bouros D, Brown KK, Colby TV, Collard HR, Cordeiro CR, Cottin V, Crestani B, Drent M, Dudden RF, Egan J, Flaherty K, Hogaboam C, Inoue Y, Johkoh T, Kim DS, Kitaichi M, Loyd J, Martinez FJ, Myers J, Protzko S, Raghu G, Richeldi L, Sverzellati N, Swigris J, Valeyre D, Pneumonias AECoII. An official american thoracic society/european respiratory society statement: Update of the international multidisciplinary classification of the idiopathic interstitial pneumonias. *American journal of respiratory and critical care medicine* 2013;188:733-748.

- Oldham JM, Noth I. Idiopathic pulmonary fibrosis: Early detection and referral. *Respiratory medicine* 2014;108:819-829.

- Selman M, Pardo A, King TE, Jr. Hypersensitivity pneumonitis: Insights in diagnosis and pathobiology. *American journal of respiratory and critical care medicine* 2012;186:314-324.

- Flaherty KR, King TE, Jr., Raghu G, Lynch JP, 3rd, Colby TV, Travis WD, Gross BH, Kazerooni EA, Toews GB, Long Q, Murray S, Lama VN, Gay SE, Martinez FJ. Idiopathic interstitial pneumonia: What is the effect of a multidisciplinary approach to diagnosis? *American journal of respiratory and critical care medicine* 2004;170:904-910.

- Ley B, Ryerson CJ, Vittinghoff E, Ryu JH, Tomassetti S, Lee JS, Poletti V, Buccioli M, Elicker BM, Jones KD, King TE, Jr., Collard HR. A multidimensional index and staging system for idiopathic pulmonary fibrosis. *Annals of internal medicine* 2012;156:684-691.