Pulmonary Manifestation of Myositis

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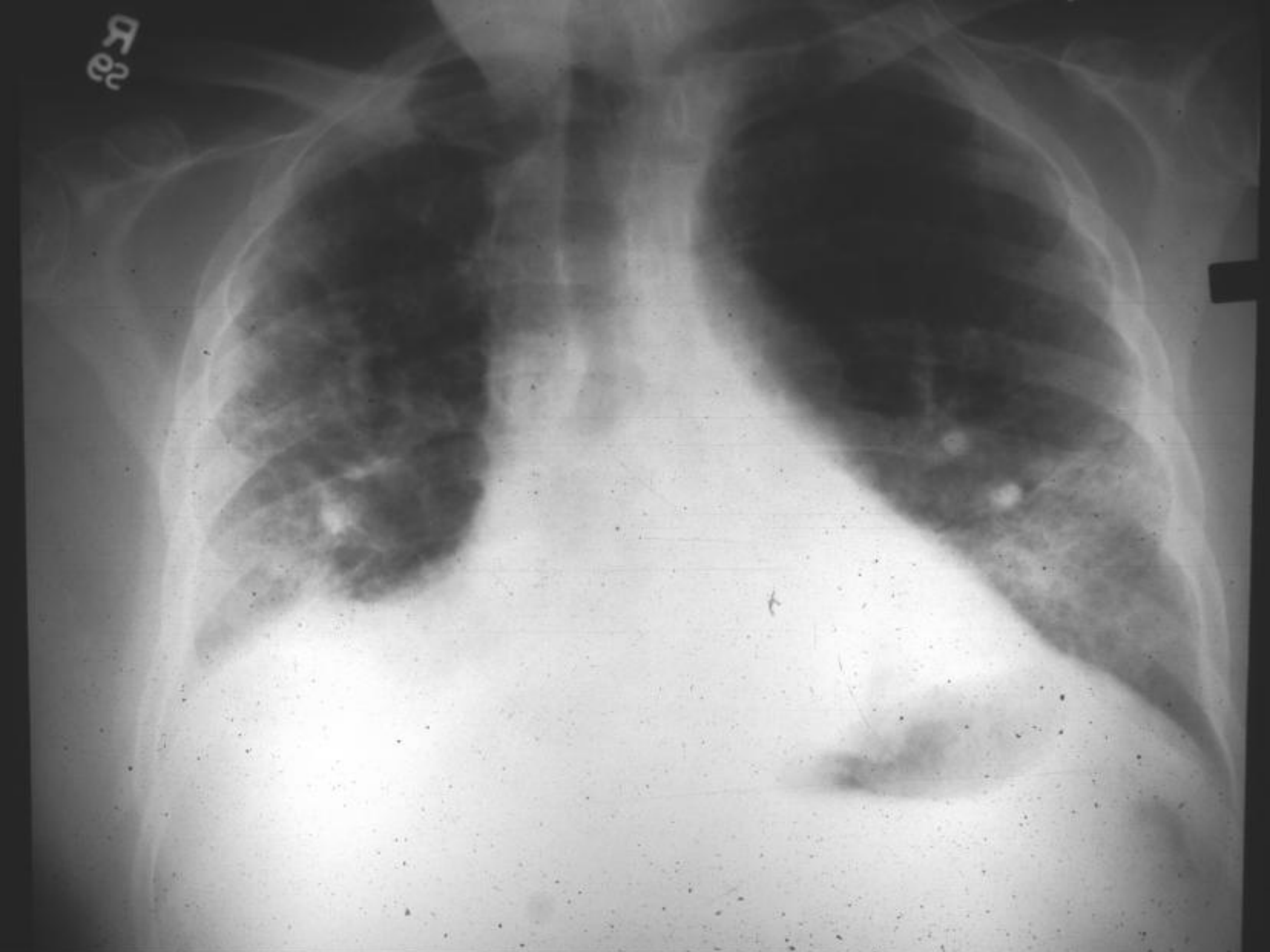
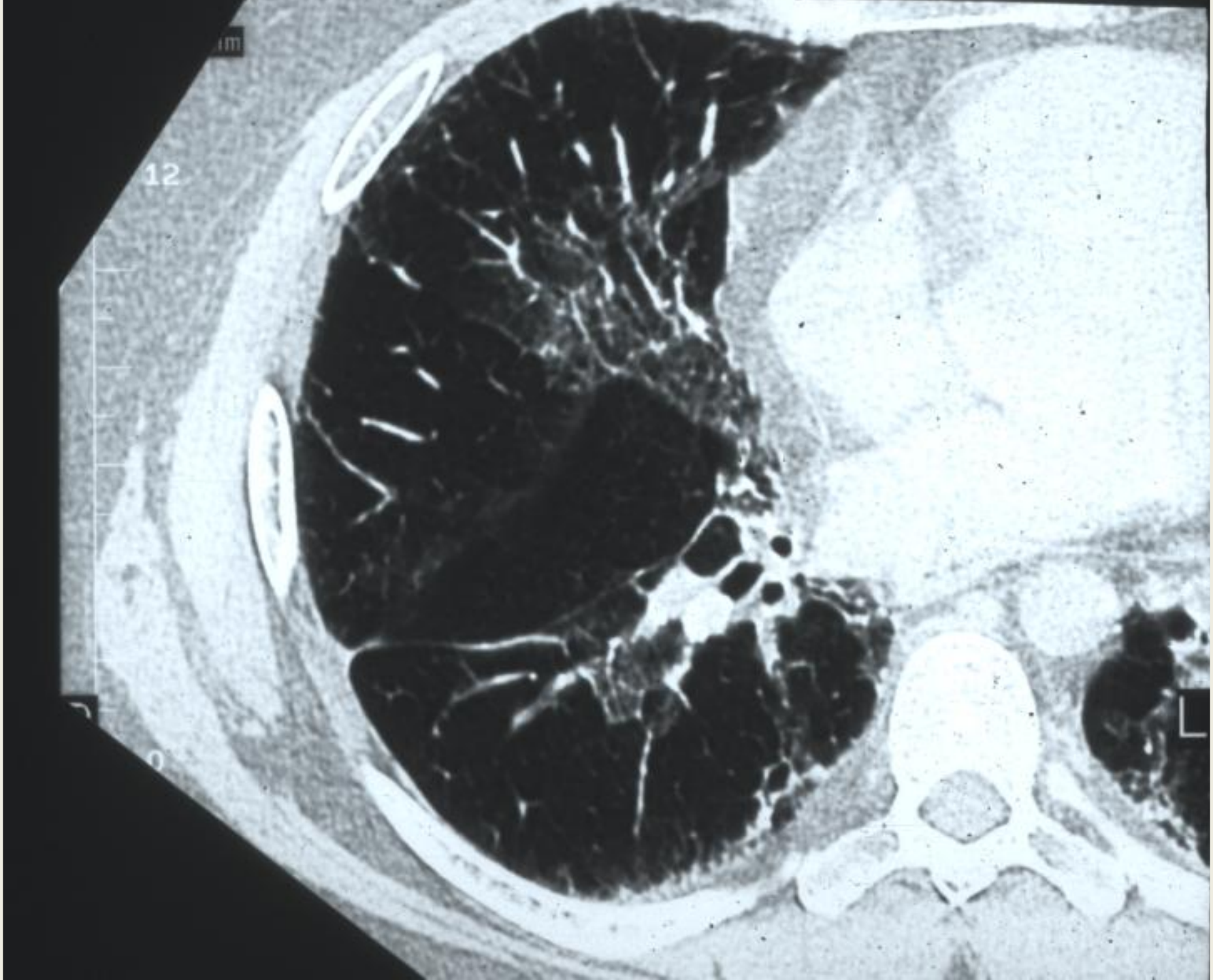
Types of Pulmonary Involvement

- Interstial lung diseases (ILD) and/or interstital pulmonary fibrosis (IPF)
  - Nmost common in patients with antisynthetase autoantibodies (I.e., anti-Jo-1)
- Diaphragmatic weakness

Diagnosis

- History and Physical Exam
- Chest X-Ray
- High Resolution Computerized Tomography (HRCT)
- Pulmonary Function Tests
- Pulse oximeter andArterial Blood Gas (ABG)
- Bronchoscopy
- Bronchoalveolar lavage (BAL)
- Surgical Lung Biopsy





Pulmonary Function Tests (PFTs)

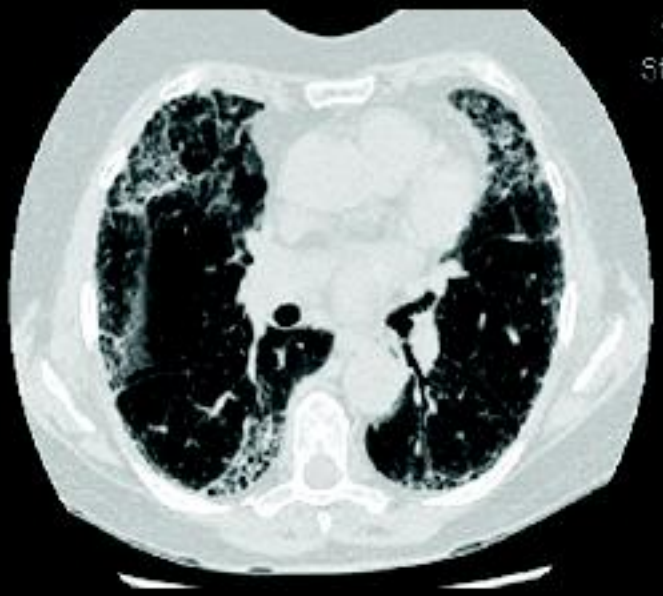
- Diffusing capacity (DLCO)
- Spirometry
  - Obstruction
  - Restriction

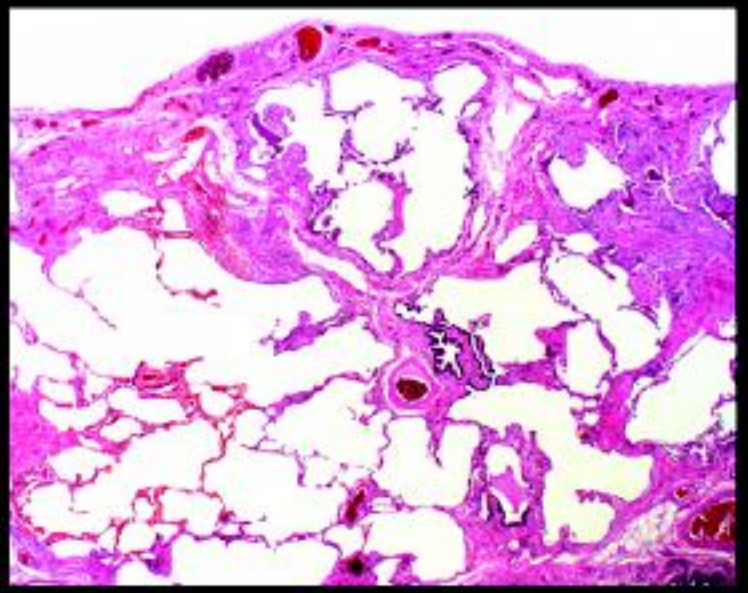
Subsets of ILD

- Usual interstitial lung disease (UID)
- Acute interstitial pneumonitis (AIP)
- Cryptogenic organizing pneumonia or bronchiolitis obliterans organizing pneumonia (BOOP)
- Desquamative interstitial pneumonia (DIP)
- Lymphocytic interstitial pneumonia (LIP)
- Nonspecific interstitial pneumonitis (NSIP)
- Respiratory bronchiolitis interstitial lung disease (RBILD)
- Diffuse alceolar damage (DAD)

Current Definition of IPF

A distinct type of chronic fibrosing interstitial pneumonia of unknown cause, limited to the lungs, and associated with a surgical lung biopsy showing a histologic pattern of UIP





ATS/ERS Consensus Statement. *Am J Respir Crit Care Med*. 2000;161:646-664; and 2002;165:277-304.

Prevalence of Idiopathic Pulmonary Fibrosis (IPF)

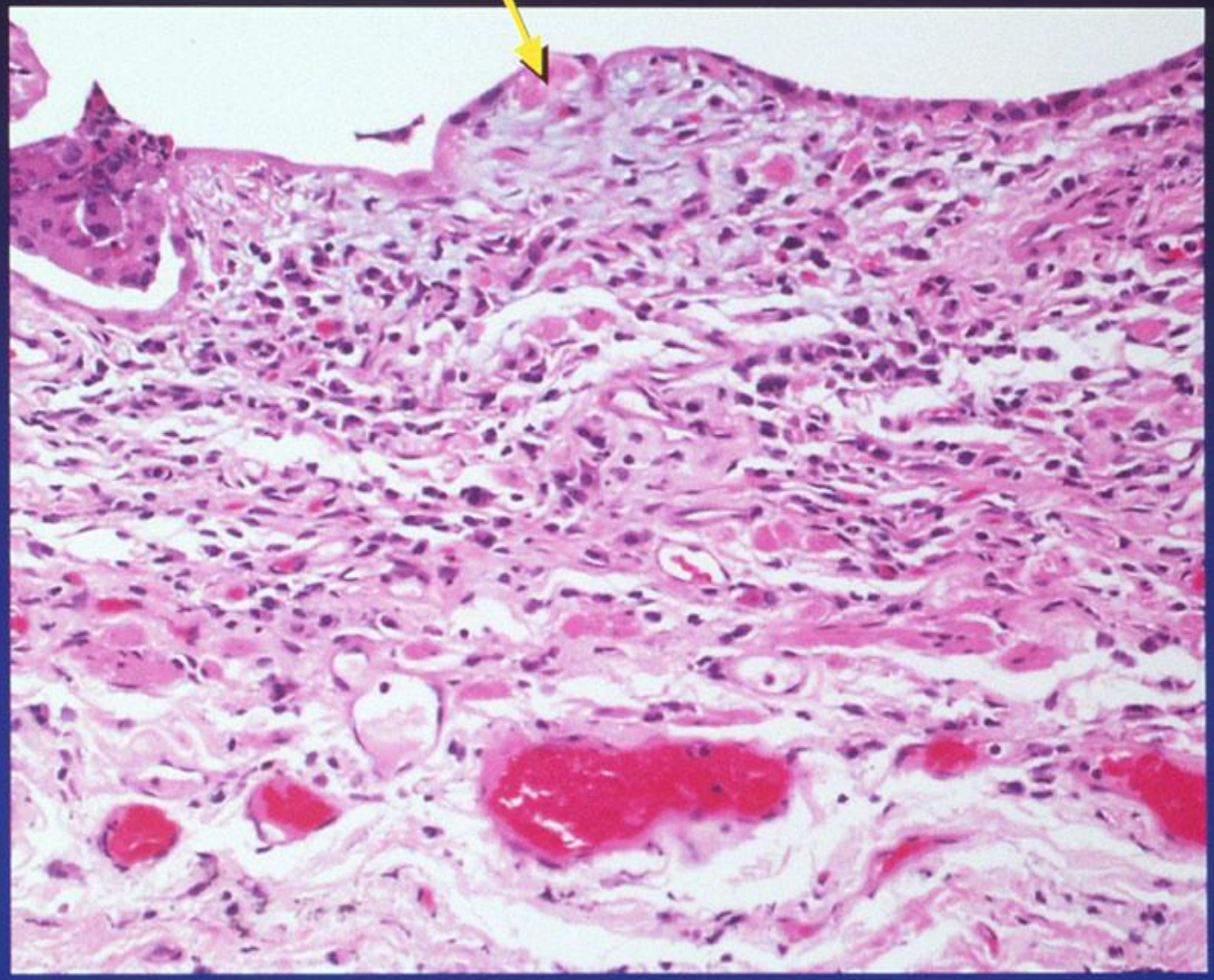
- 128,000 to 200,00 people in the US
- Associations
  - None
  - Polymyositis and Dermatomyositis
  - Rheumatoid arthrtis
  - Systemic lupus erythematosus
  - Scleroderma
  - Sjogren's syndrome
  - Mixed Connective tissue disease

Symptoms

- Shortness of breath
- Chronic dry, hacking cough
- Fatigue and weakness
- Discomfort in the chest
- Loss of appetite
- Rapid weight loss

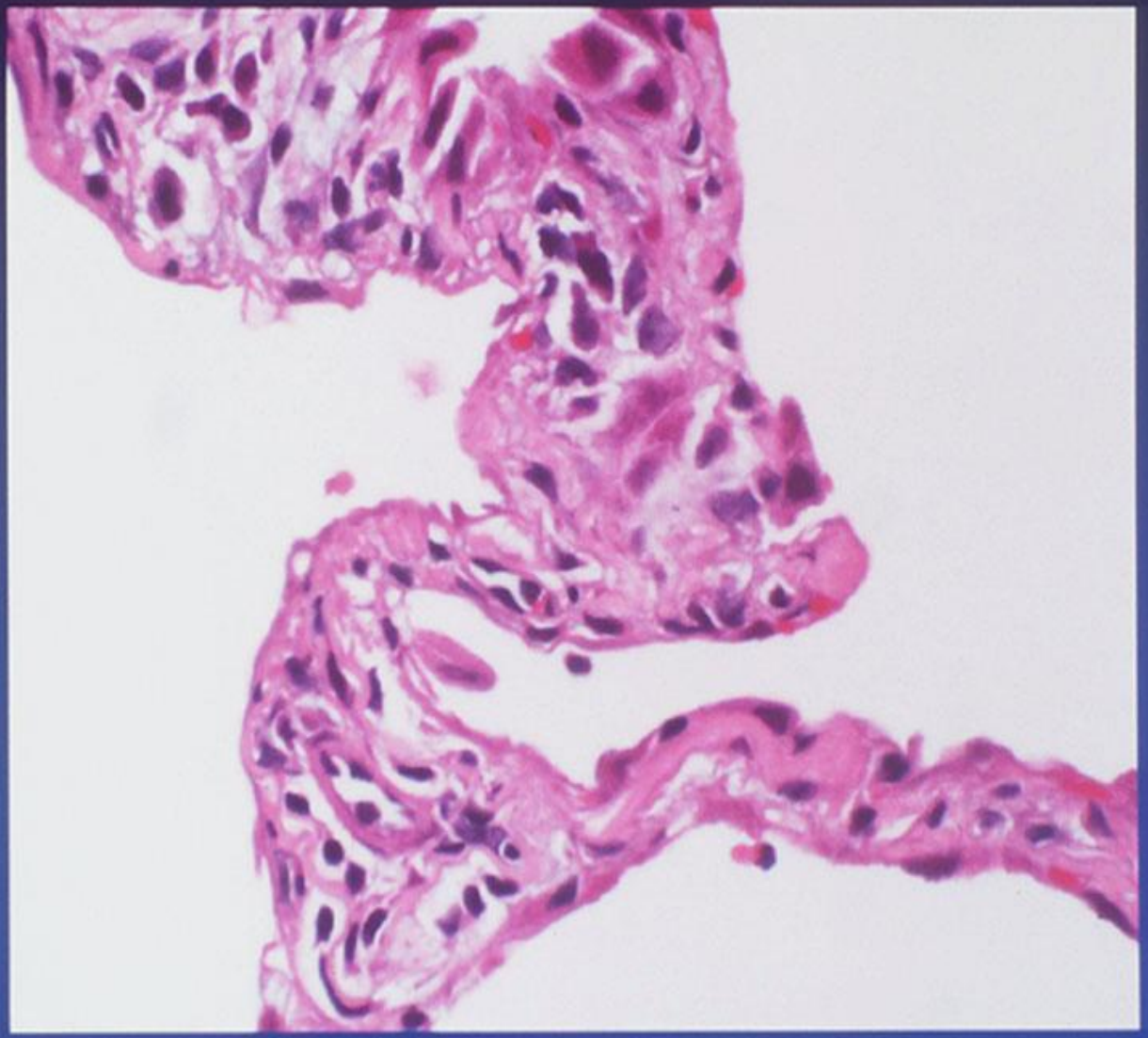
Pathology of UIP/IPF

Leading Edge of "Fibroblastic Foci"

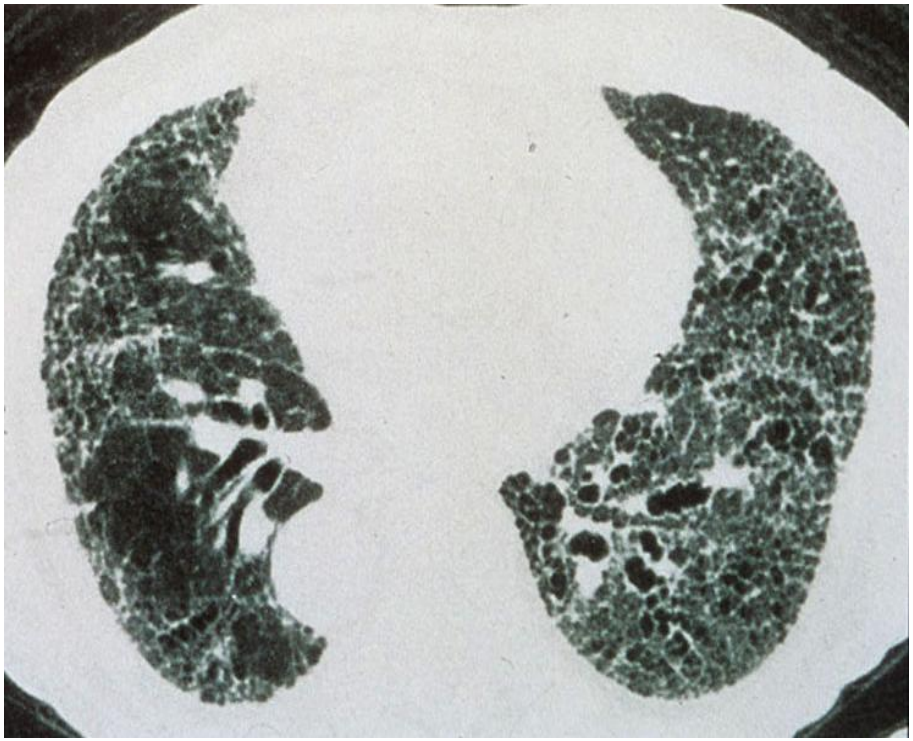


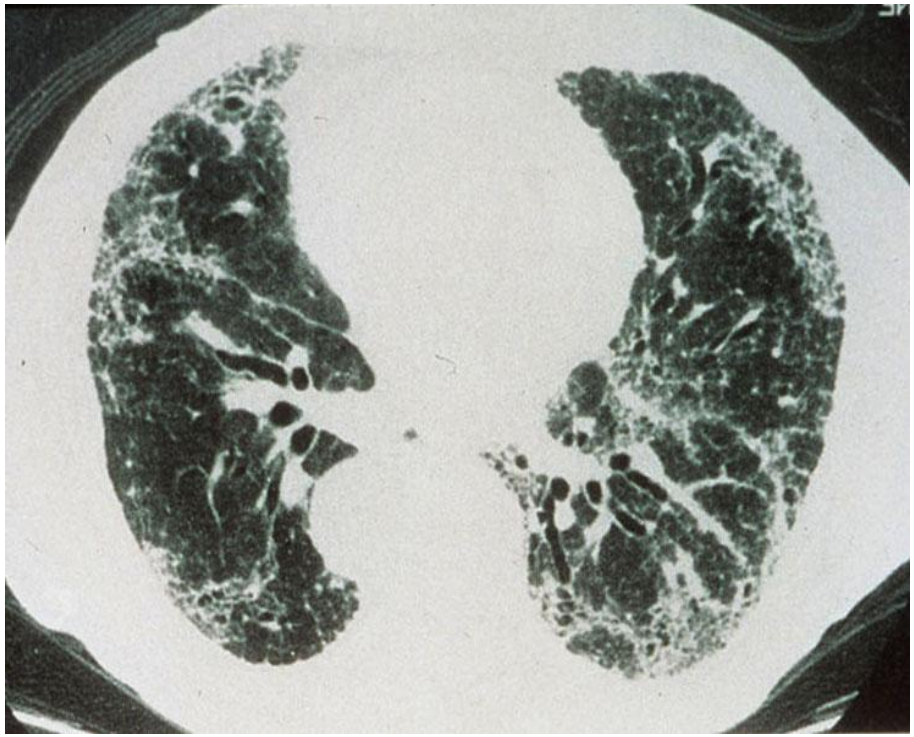
Pathology of UIP/IPF

Patchy Interstitial Chronic Inflammation



HRCT FINDINGS IN IPF

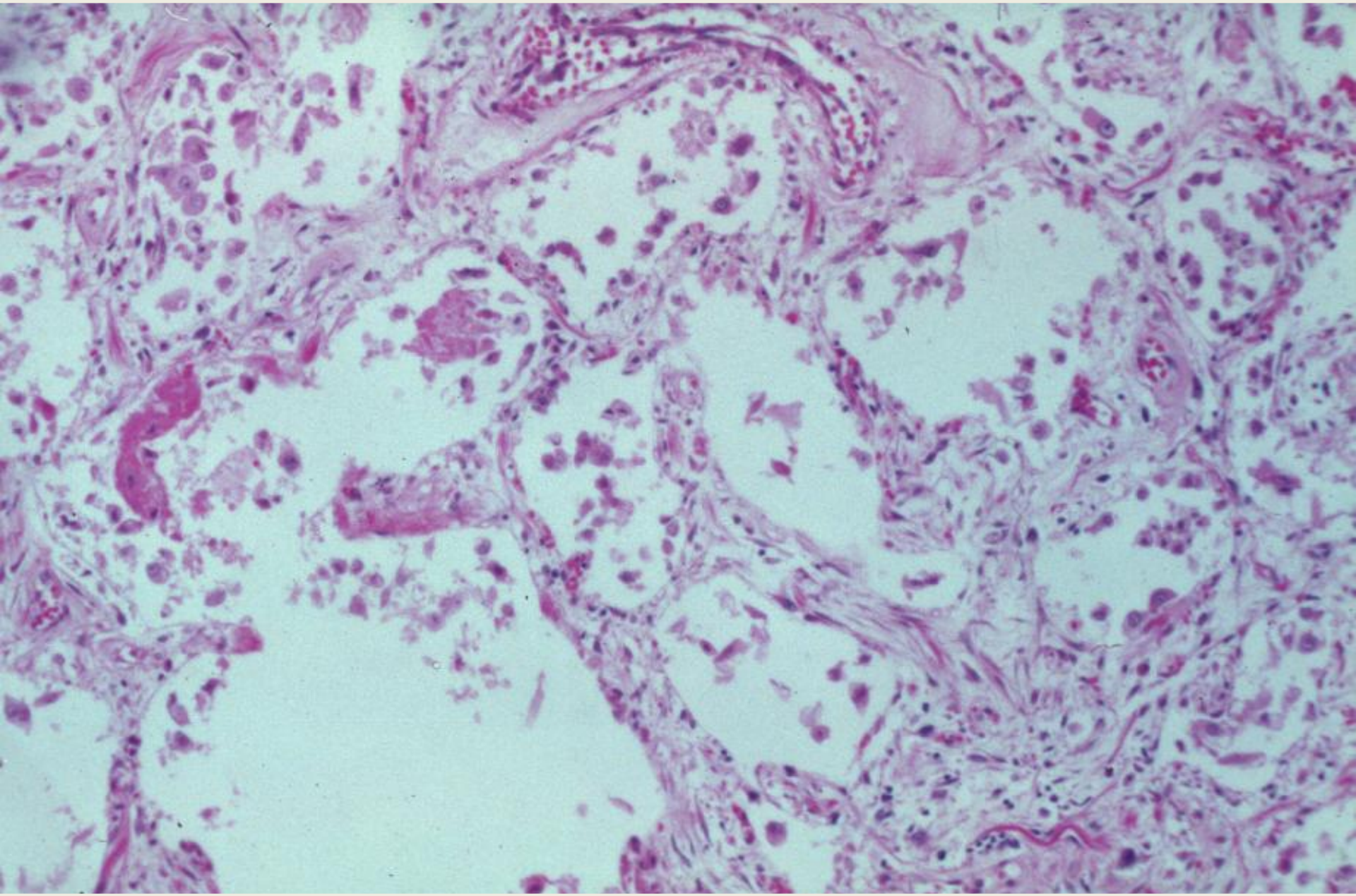




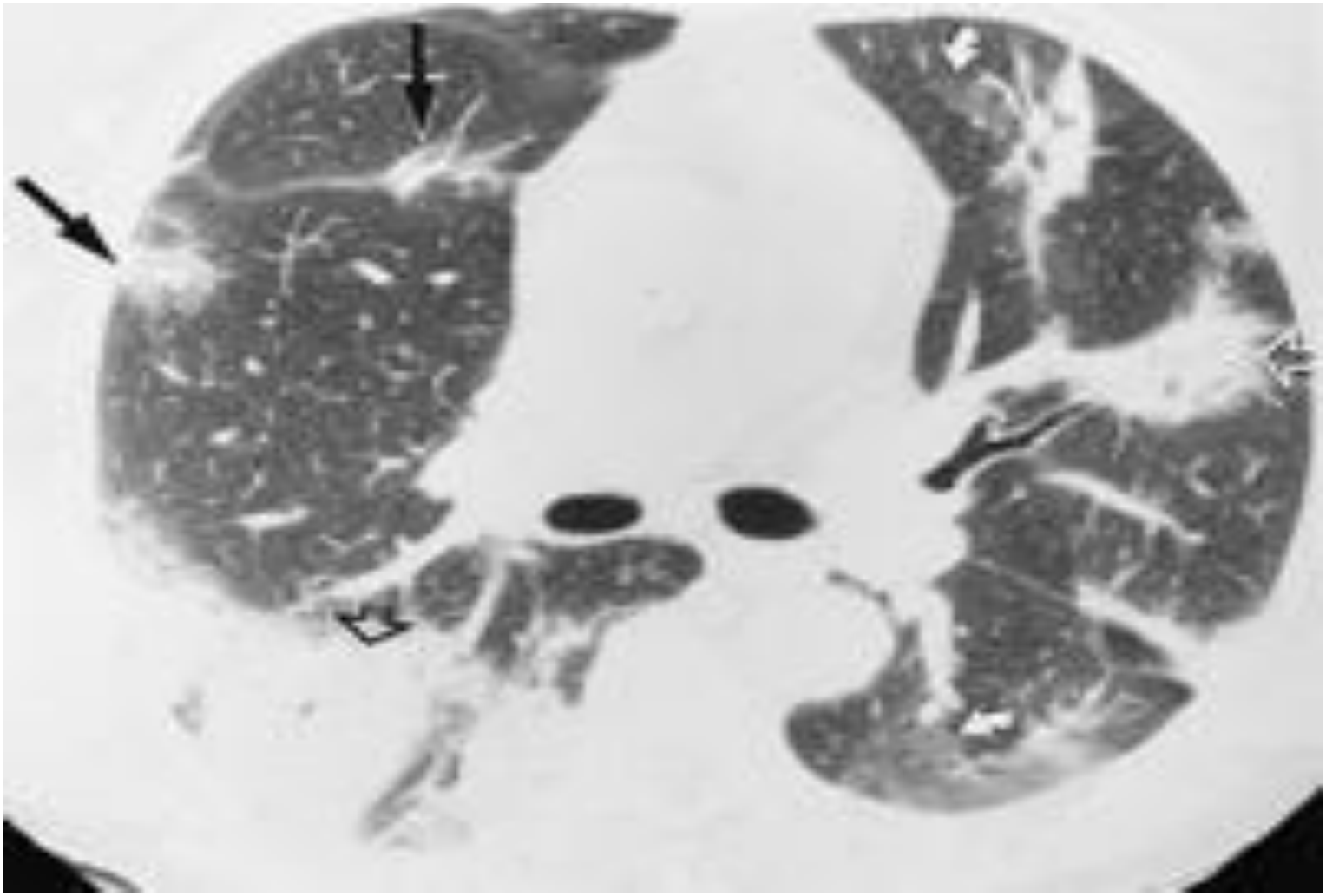
CLINICAL AND PATHOLOGIC FEATURES OF AIP AND UIP/IPF

	AIP	UIP/IPF
Clinical Features		
Onset	Acute	Insidious
Course	Fulminant (4-6 wks)	Slowly progressive (3-5 yrs)
5 yr Mortality	60 - 90%	> 60%
Complete recovery possible	Yes	No
Pathologic Features		
Temporal appearance	Uniform	Variegated
Fibroblasts	Diffuse	Focal (Fibroblast foci)
Hyaline membranes	Focal	Absent
Thrombi	Focal	Absent

Hamman and Rich, Bull Johns Hopkins Hosp 74:177, 1944
Carrington, et al. N Engl J Med 298:801, 1978
Katzenstein, et al. Am J Surg Pathol 10:256, 1986



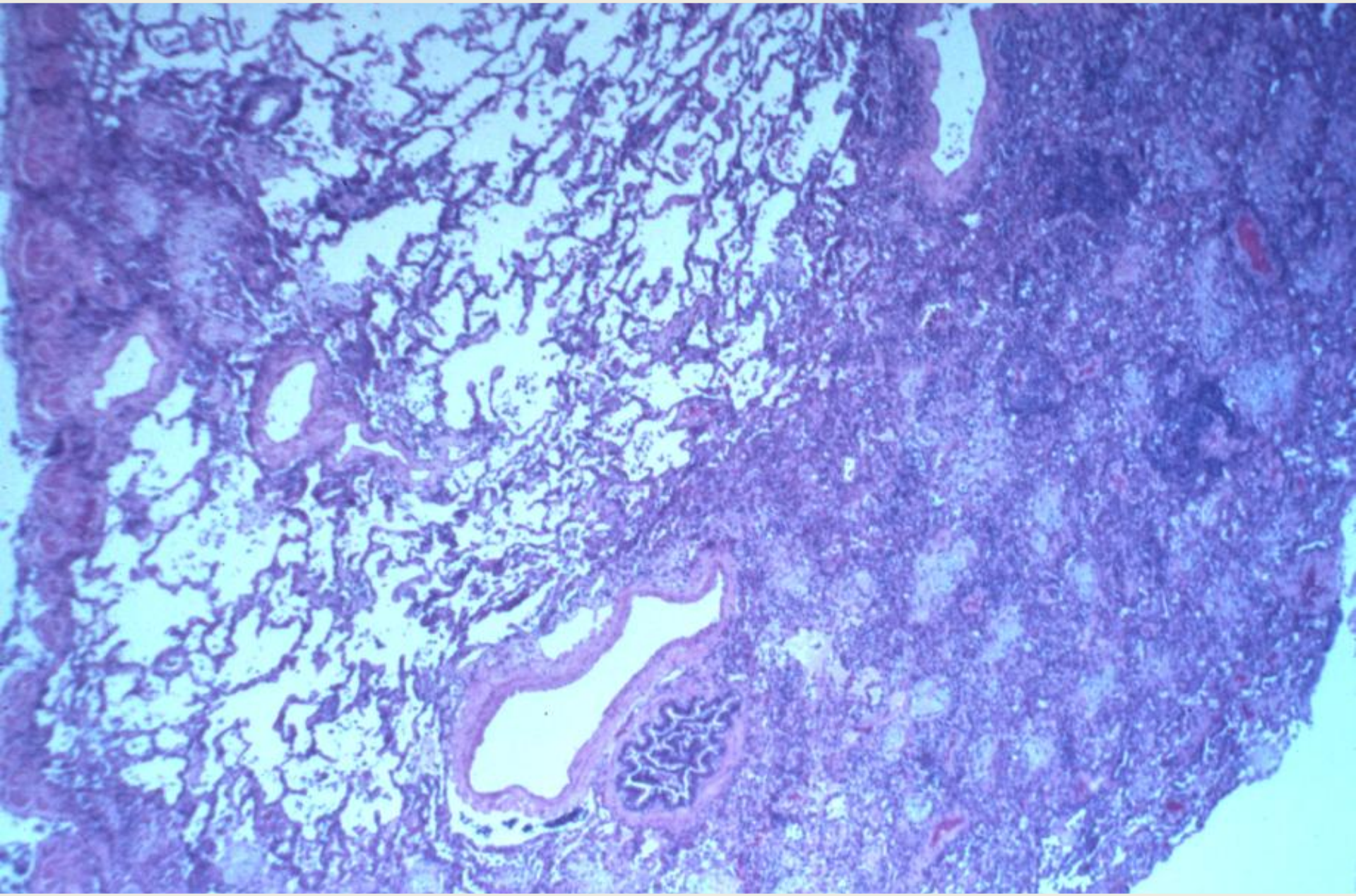
Cryptogenic Organizing Pneumonia



CLINICAL AND PATHOLOGIC FEATURES OF UIP/IPF AND BOOP/COP

	UIP/IPF	BOOP/COP
Clinical Features		
Onset	Insidious	Acute
Systemic symptoms	Infrequent	Common
Chest radiograph	Bilateral interstitial	Usually patchy airspace
Treatment	Steroids, cytoxan, or azathioprine	None or steroids
Prognosis	Poor	Excellent
Pathologic Features		
Temporal distribution	Heterogeneous	Uniform
Septal fibroblast foci	Extensive	Mild
Intraluminal fibrosis	Mild/moderate	Extensive

Katzenstein, et al. Am J Surg Pathol 10:373, 1986
Guerry-Force, et al. Am Rev Respir Dis 135:705, 1987
Cordier, et al. Chest 96:999, 1989

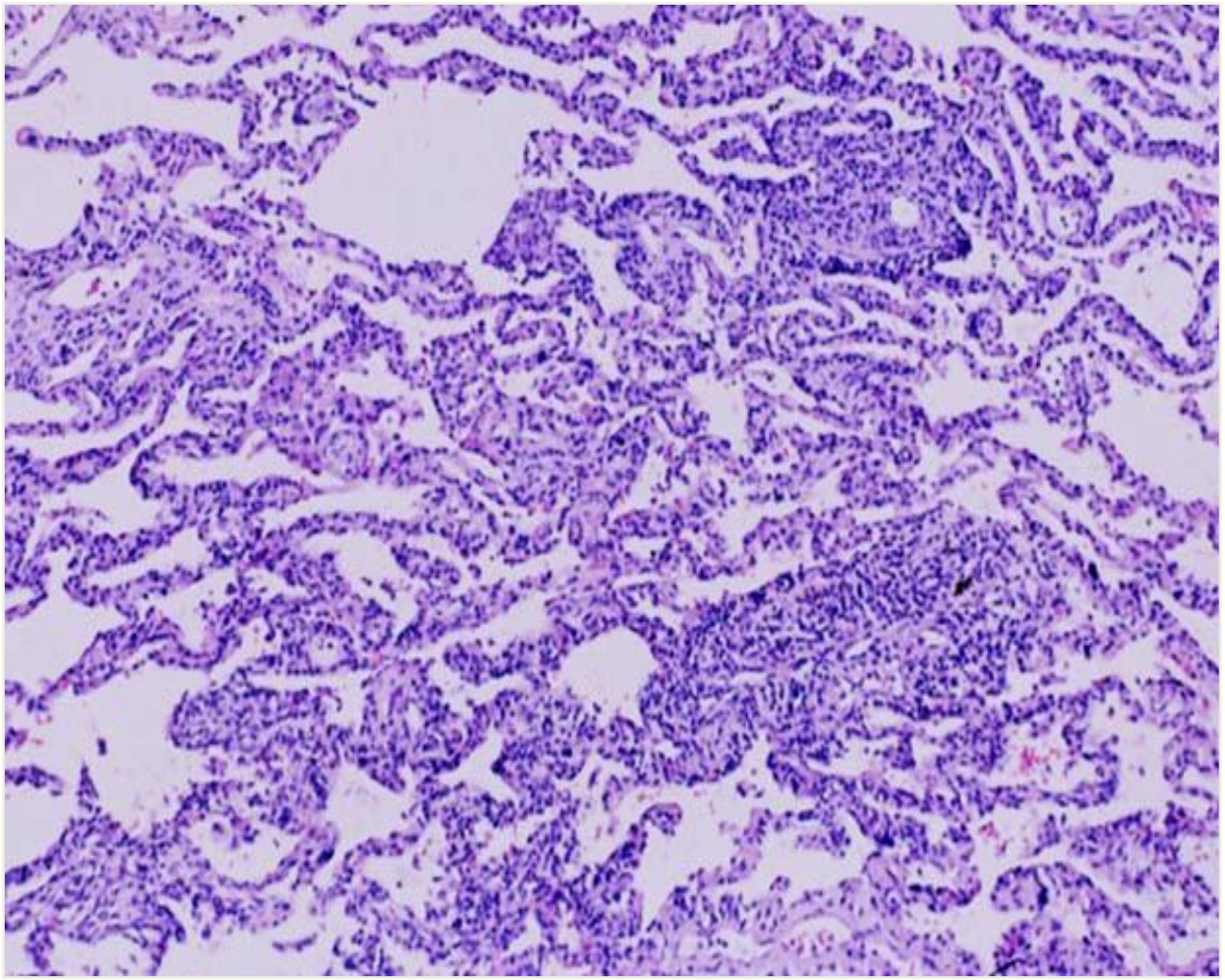


Nonspecific Interstitial Pneumonia/Fibrosis

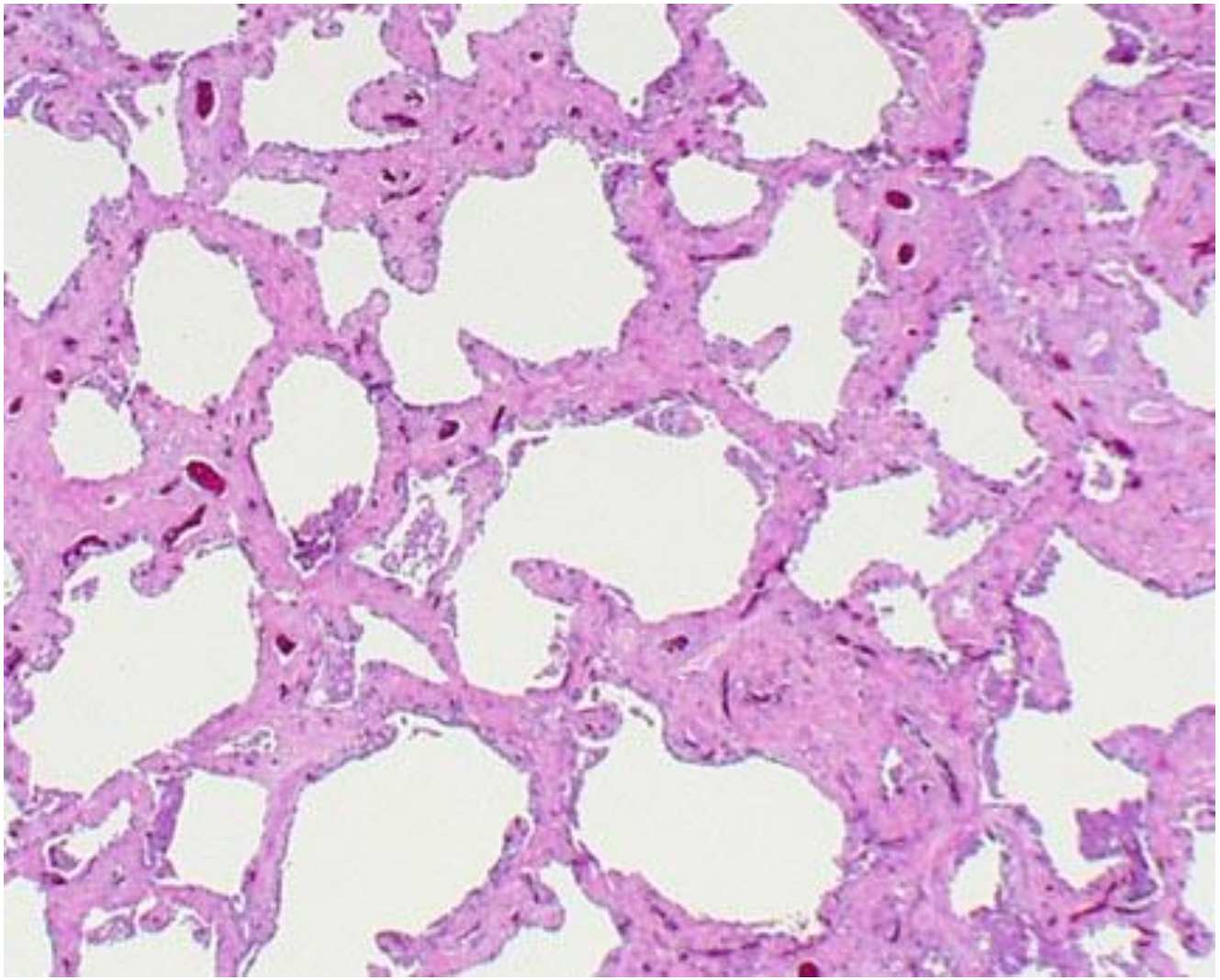
- F>M (1.5:1); mean 5th decade (range 9-78)
- Dyspnea, cough, fever: mean duration 8 months (range 1 week to 5 years)
- Associated/underlying conditions
  - Collagen vascular disease (10/64)
  - Organic antigen exposure (10/64)
- Prognosis generally good
  - >90% 5 year survival

Katzenstein, AL, Am J Surg Pathol. 18:1994

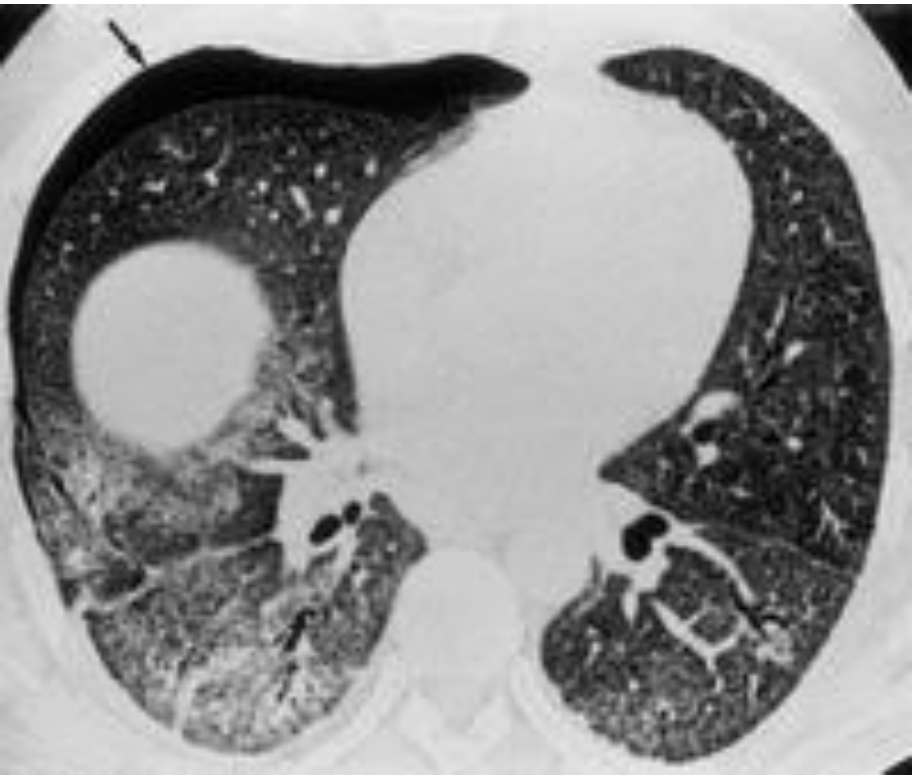
Cellular NSIP

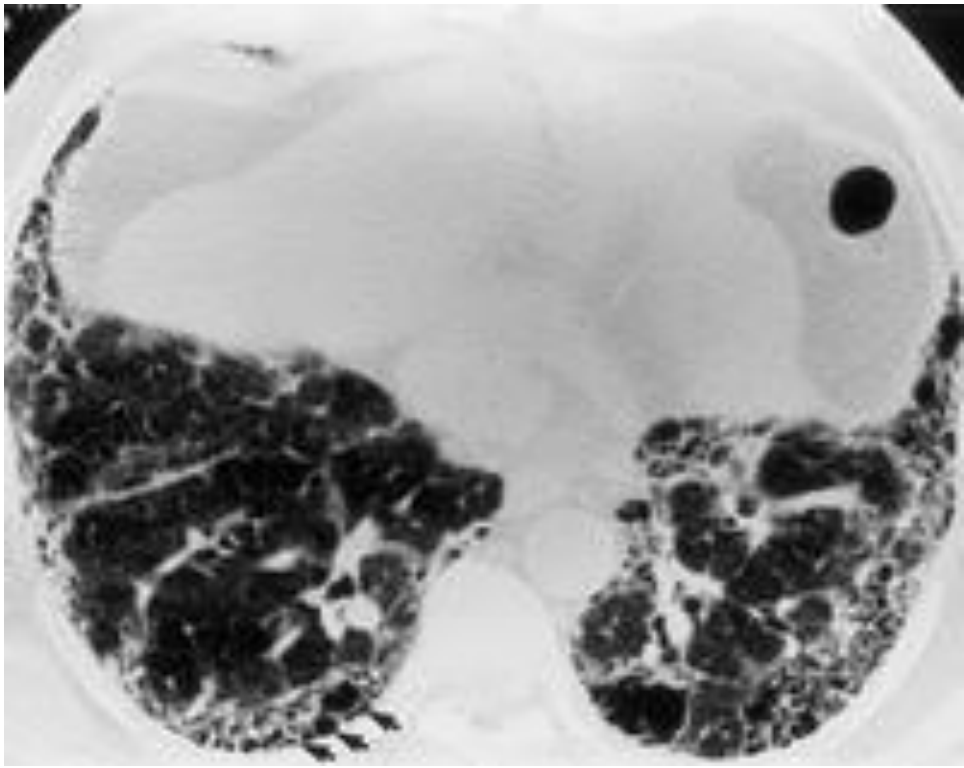


Fibrotic NSIP



HRCT in Cellular vs. Fibrotic NSIP





Histopathologic Variability in UIP and NSIP

- 168 surgical lung biopsies for IIP (Michigan)
- 109 had multiple lobes sampled
  - 3 blinded pathologists: each lobe diagnosed
  - 28 % were discordant
  - No lobar predilection for either diagnosis
  - Survival reflected the worst diagnosis

Flaherty, K.R., et al. Am J Respir Crit Care Med. 2001

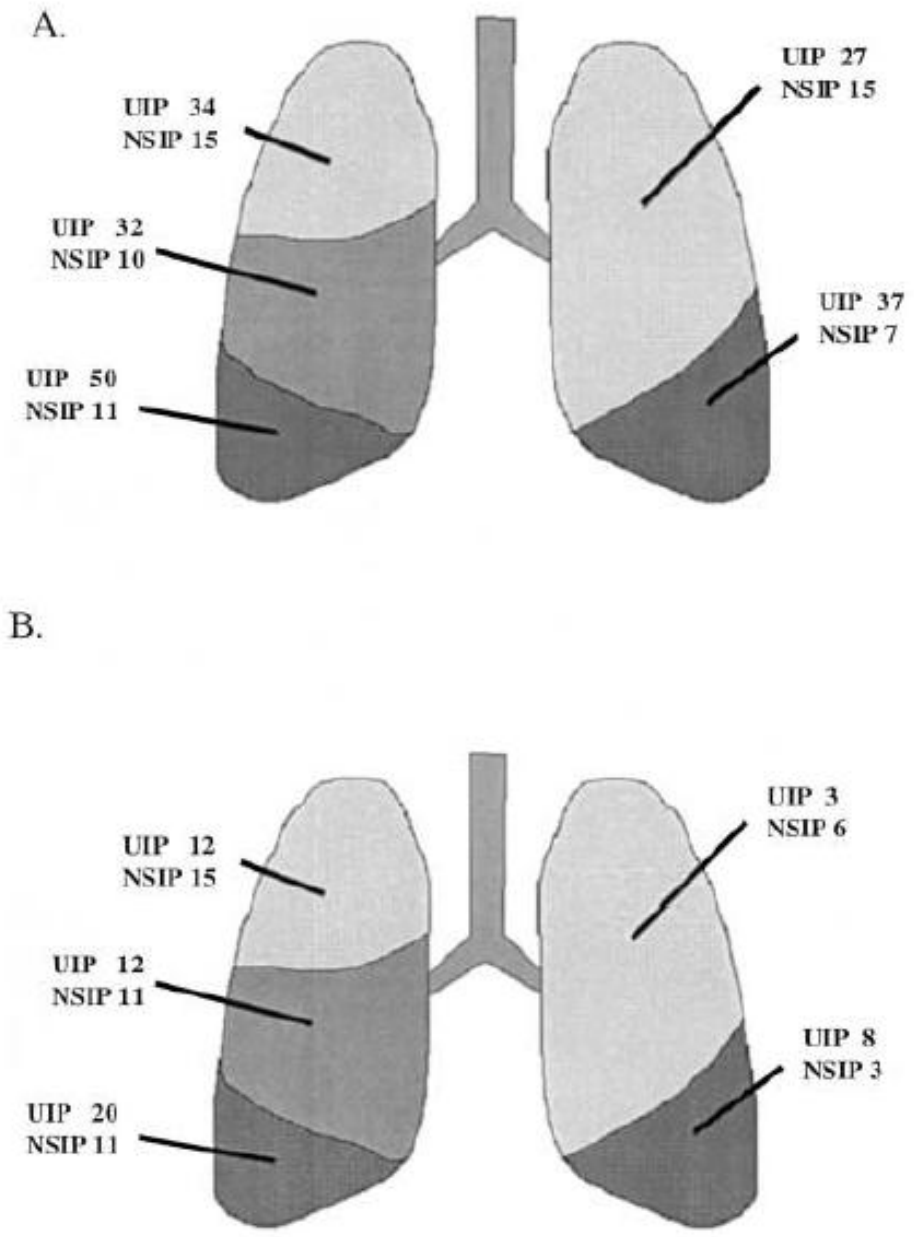


Figure 1. (*A*) Lobar histologic diagnosis in 109 patients with UIP or NSIP. (*B*) Lobar histologic diagnosis in 28 patients with a UIP pattern in at least one lobe but an NSIP pattern in at least one lobe (discordant UIP).

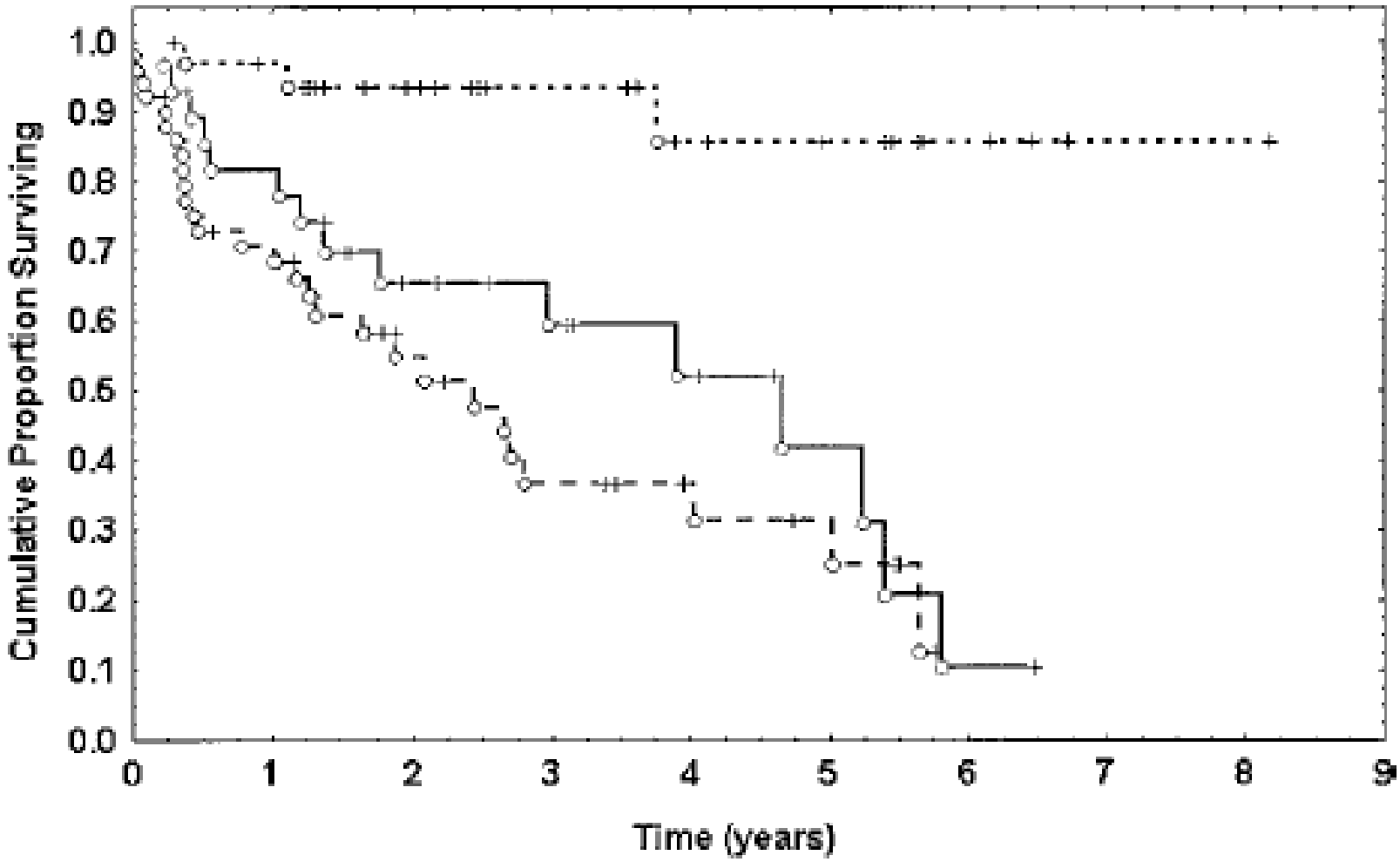
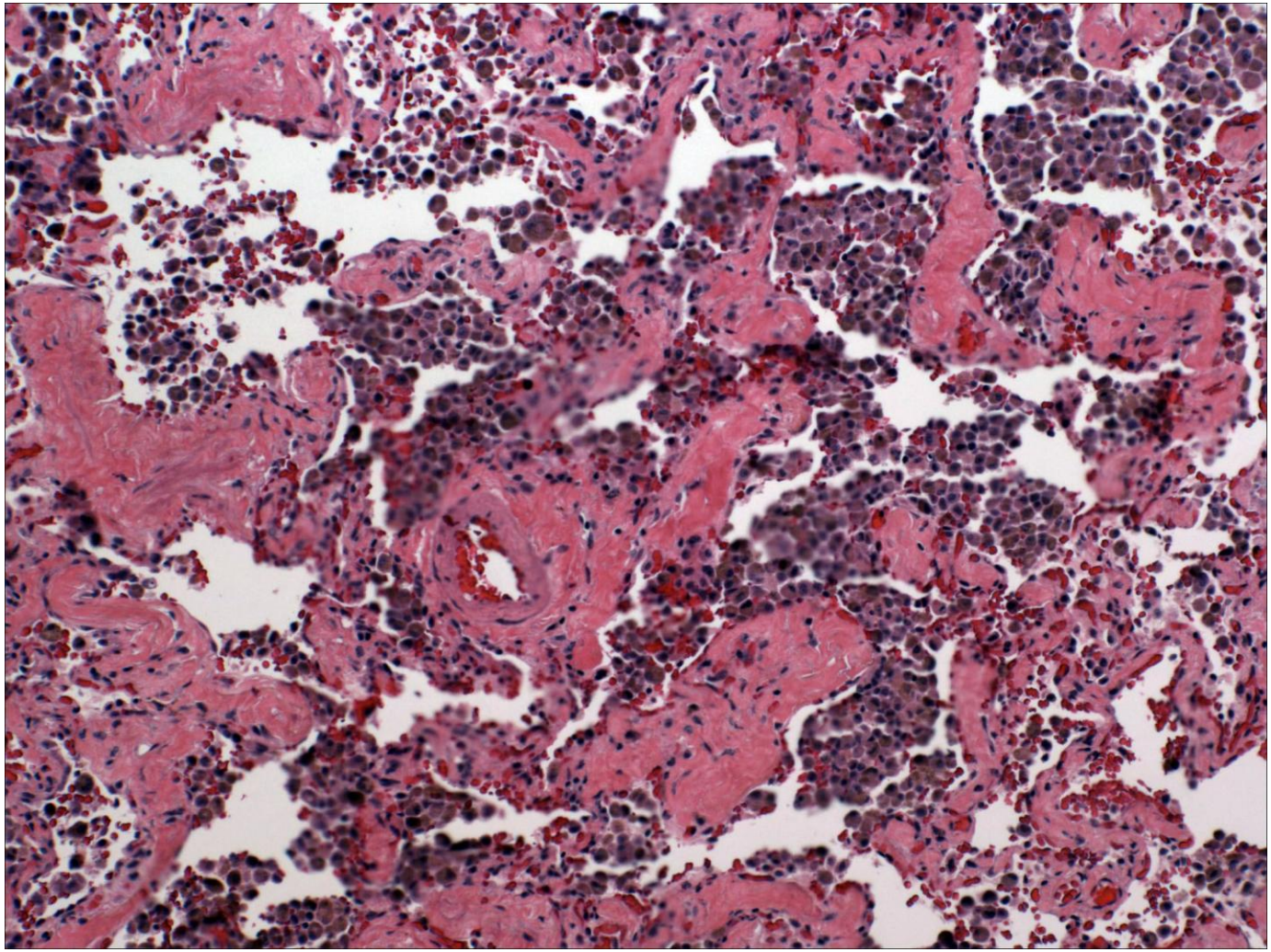


Figure 2. Kaplan–Meier survival curves for patients with concordant UIP (n = 51), discordant UIP (n = 28), and NSIP (n = 30), grouped by histologic classification ($p < 0.0003$). (*dotted line*: NSIP; *solid line*: discordant UIP; *dashed line*: concordant UIP; +: last follow up visit; o: death).

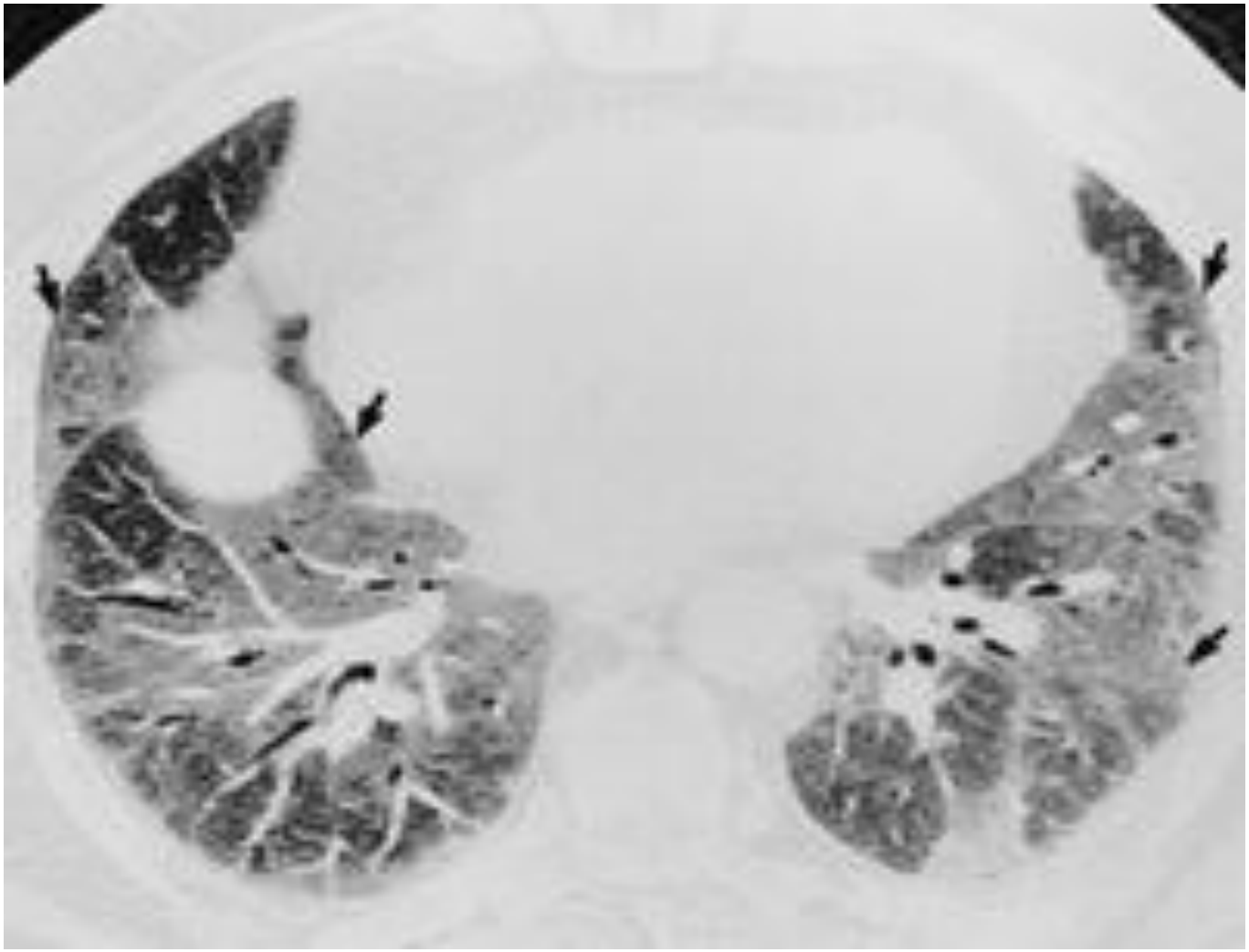
Diffuse Alveolar Damage

- Infection (viral, bacterial, fungal)
- Toxic inhalations
- Drugs
- Radiation reaction (acute)
- Alveolar hemorrhage syndromes
- Vasculitis
- Connective tissue disease
- Idiopathic (AIP)

DIP/RBILD



DIP/RBILD: HRCT



CLINICAL AND PATHOLOGIC FEATURES OF UIP/IPF AND DIP

	UIP	DIP
Clinical Features		
Mean age	55 yr	42 yr
Spontaneous improvement	No	Occasionally
Response to steroids	<10%	>60%
Mortality (mean survival)	>60% (4-5 yr)	27% (12 yr)
Pathologic Features		
Temporal distribution	Heterogeneous	Uniform
Fibroblast foci	Extensive	Minimal
Intraalveolar macrophages	Focal	Diffuse

Carrington, et al. N Engl J Med 298:801, 1978
Katzenstein, et al. Am J Surg Pathol 10:373, 1986

PM/DM-Associated ILD
(Douglas. AJRCCM 2001;164:182)

- NSIP-cellular 32%
- NSIP-cellular and fibrotic 41%
- NSIP-fibrotic 10%
- UIP 4%
- DAD 9%
- BOOP 4%

PM/DM-Associated ILD
(Douglas. AJRCCM 2001;164:182)

- Lung disease was presenting feature in 30%
- Steroid response may delay correct diagnosis of PM/DMM
- Muscles respond faster than lungs to treatment
- Incomplete resolution of pulmonary infiltrates is common

Management

- Corticosteroids: (Prednisone)
- Cyclophosphamide (Cytoxan)
- Azathioprine (Imuran)
- N-acetylcysteine (NAC)
- Tacrolimus
- Mycophenolate (Cellcept)
- Cyclosporine
- Supplemental Oxygen Therapy
- Pulmonary
- Lung Transplantation