Interstitial lung diseases

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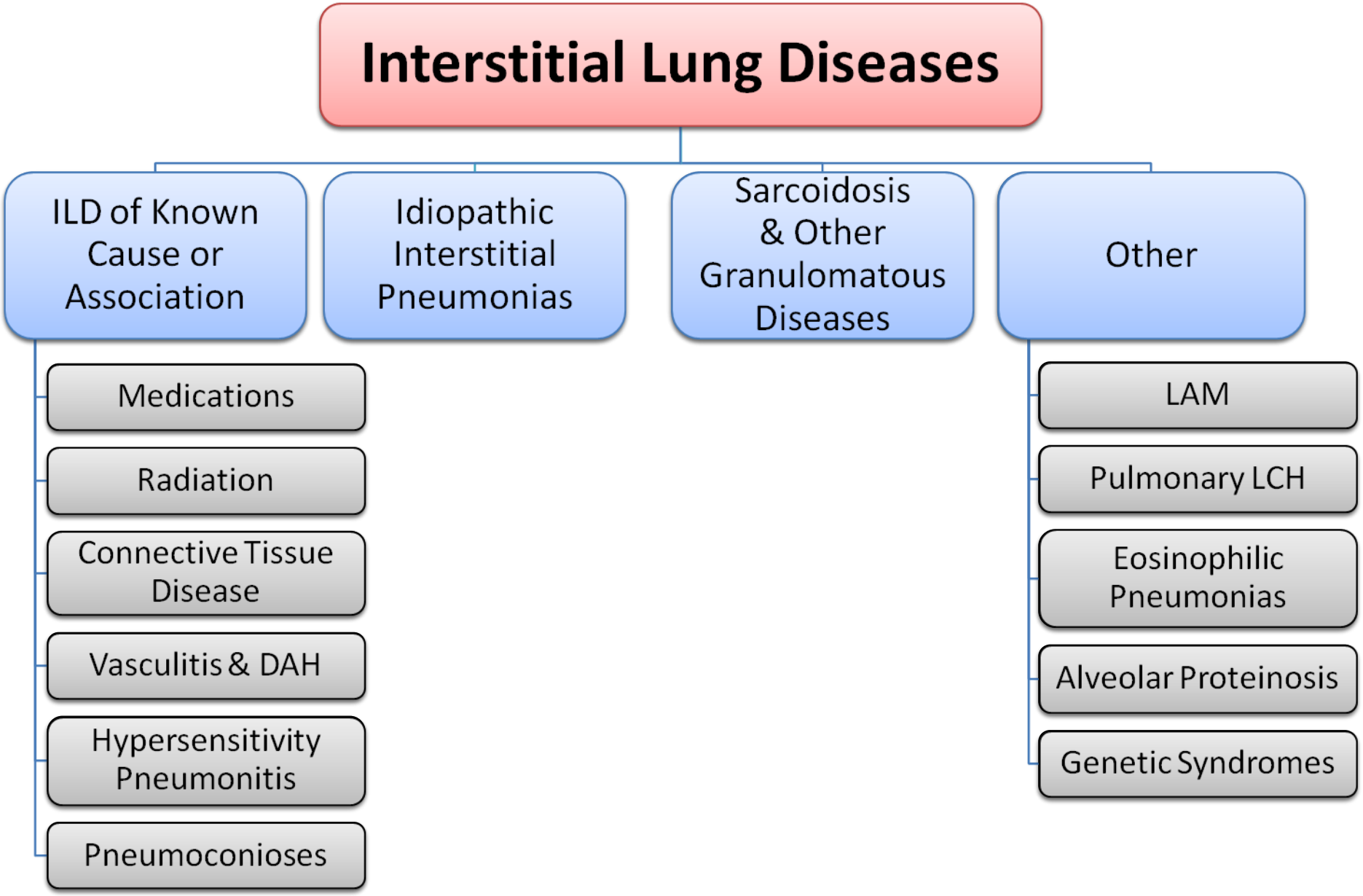
Interstitial Lung Diseases - Difficulties

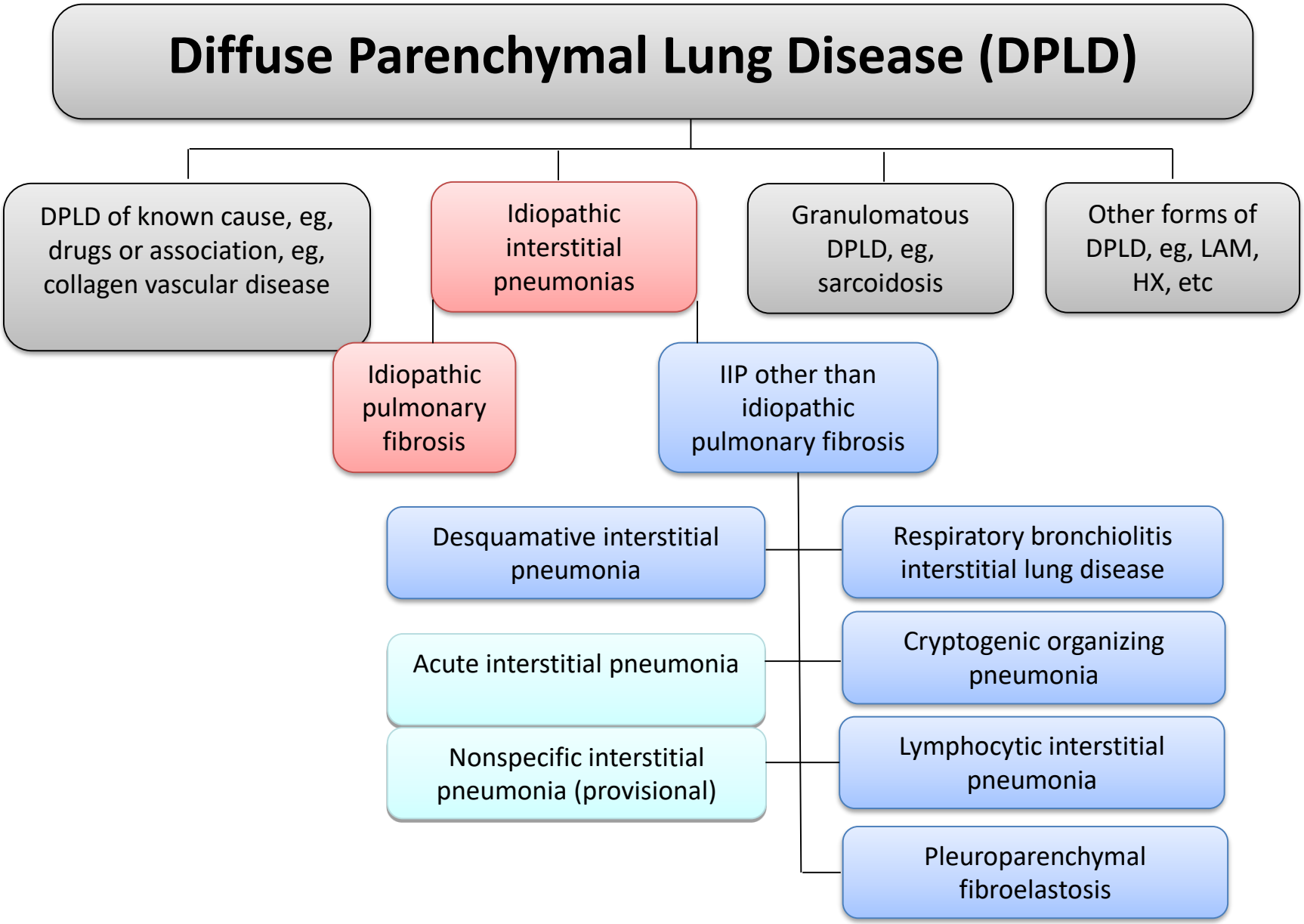
- Diverse group of disorders (130+)
- Involve the distal pulmonary parenchyma by varying patterns of inflammation and fibrosis.
- Similar symptoms, physiology, radiology
- Difficult nomenclature
- Limited, often toxic, treatments

Interstitium

- The interstitium includes the space between the epithelial and endothelial basement membranes and it is the primary site of injury.



Adapted from: ATS/ERS Guidelines for IIP. *AJRCCM*. 2002;165:277-304.



Travis WD, et al; ATS/ERS Committee on Idiopathic Interstitial Pneumonias. *Am J Respir Crit Care Med*. 2013;188(6):733-748.

Clinical Evaluation

- The approach to patients with diffuse parenchymal lung disease begins with a careful history followed by physical examination, routine chest radiographs, and pulmonary function testing .

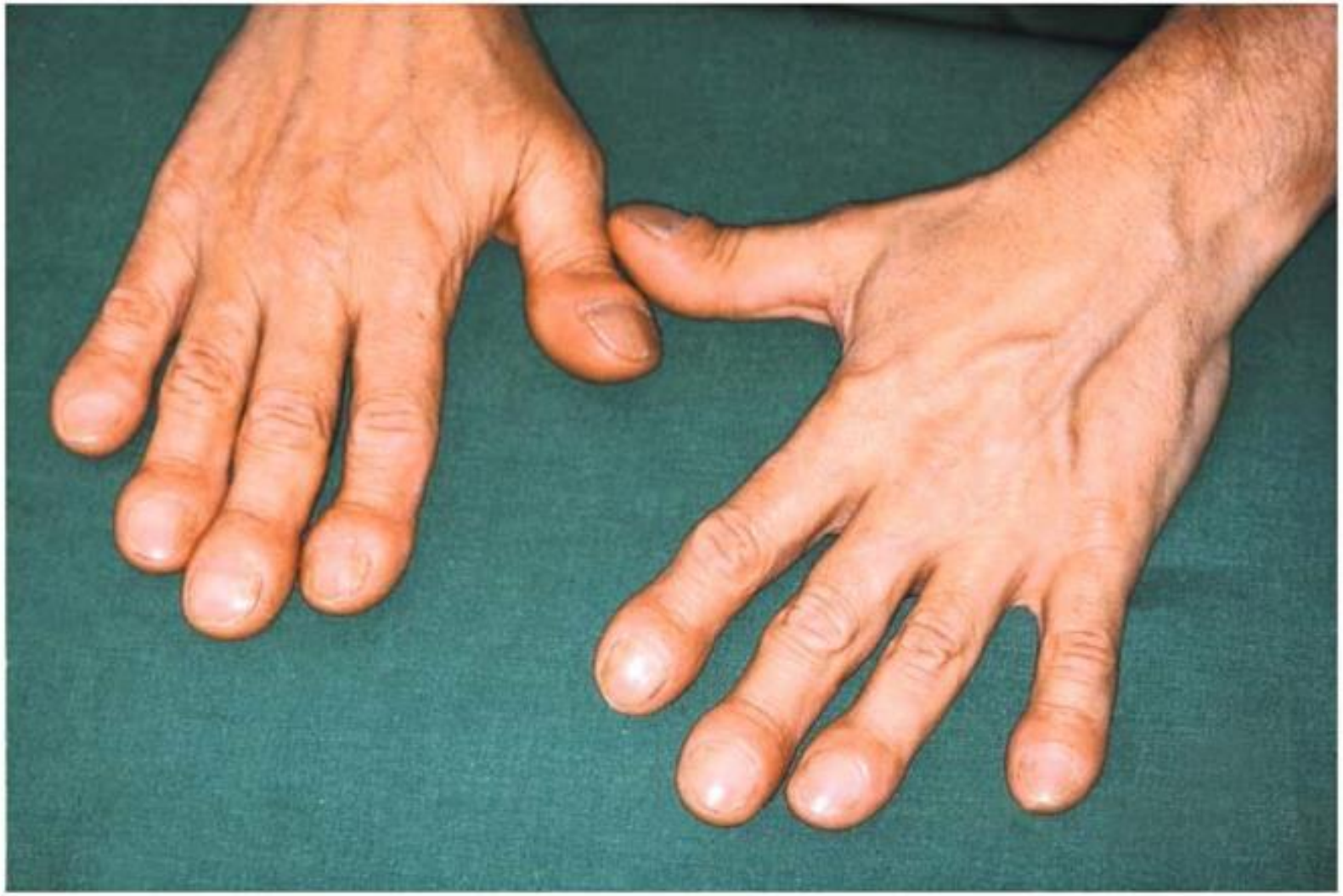
- The assessment of the clinical history should include the nature of the first symptoms (usually breathlessness or cough), their progression, clinical course, and in particular the presence of comorbid disease such as collagen vascular disease.

- A record of environmental exposures including smoking status, drug use, and detailed occupational exposures with dates, duration of exposure.

Physical examination

- crackles
- finger clubbing may be present
- joint swelling or tight skin may suggest collagen vascular disease

Digital Clubbing



Reynen K, et al. *N Engl J Med.* 2000; 343:1235

ILD Features

Similar	Different

• Dyspnea
  – Progressive
  – Exertional
• Cough
  – Non-productive
• Bibasilar crackles
• Restrictive ventilatory defect
• Exertional desaturation
• ILD on HRCT
	• Prior/current exposures
	• Extrapulmonary findings
	  – Sarcoidosis
	  – Connective tissue disease
	  – Joint involvement
	• Serologies
	• HRCT
	  – Honeycombing
	  – Ground glass
	  – Distribution of abnormalities
	• Histopathology

Pulmonary Function Tests

- PFTs show restriction (with low lung volumes) and reductions in diffusion capacity that correlate with the extent of disease on HRCT

- Hypoxemia is a universal finding at later stages of the disease and worsens as the disease progresses.

High Resolution CT scan

Allows detailed evaluation of the lung parenchyma

- Technique
  - Does NOT use contrast
  - Thin collimation
    - HRCT, approximately 1 mm slice thickness
    - Conventional CT, approximately 10 mm

http://www.pfdoc.org/2013/08/should-i-undergo-lung-biopsy-to.html. Accessed August 2014.

Serological Evaluation

- Minimum: ANA (atinuclear antibodies), RF, CCP (anticitrulin antibodies) (ATS/ERS guidelines)

- Based on history & physical exam, consider:
  - Extractable nuclear antigen (ENA) autoantibody panel
  - CRP
  - MPO/PR3 (ANCA) antibodies
  - Anti-cardiolipin antibodies, lupus anticoagulant
  - Creatine kinase,
  - Hypersensitivity pneumonitis panel
- Should be performed before a biopsy

Idiopathic interstitial pneumonias

- *Idiopathic* indicates unknown cause and *interstitial pneumonia* refers to involvement of the lung parenchyma by varying combinations of fibrosis and inflammation, in contrast to airspace disease typically seen in bacterial pneumonia.

- Annual incidence rates of 31.5 per 100,000 person/yr in males and 26.1 per 100,000person/yr in females.

- Lung biopsies are not frequently obtained from patients with clinical evidence of interstitial lung disease, because many patients with these diseases are viewed as too old or too frail to undergo biopsy.

Major Idiopathic Interstitial Pneumonias

Category	Clinical-Radiologic-Pathologic Diagnosis	Associated Radiographic and/or Pathologic pattern
Chronic fibrosing	IPF	UIP
	Idiopathic nonspecific interstitial Pneumonia (iNSIP)	NSIP
Smoking-related	Respiratory bronchiolitis-ILD (RB-ILD)	Respiratory bronchiolitis
	Desquamative interstitial pneumonia (DIP)	Desquamative interstitial pneumonia
Acute/ subacute	Cryptogenic organizing pneumonia (COP)	Organizing pneumonia
	Acute interstitial pneumonia (AIP)	Diffuse alveolar damage

Travis et al. *Am J Respir Crit Care Med.* 2013;188:733-748.

Other Idiopathic Interstitial Pneumonias

Category	Clinical-Radiologic-Pathologic Diagnosis	Associated Radiographic and/or Pathologic pattern
Rare	Idiopathic lymphoid interstitial pneumonia (iLIP)	Lymphoid interstitial pneumonia
	Idiopathic pleuroparenchymal fibroelastosis (IPPFE)	Pleuroparenchymal fibroelastosis
Unclassifiable	Unclassifiable IIP	Many

Travis et al. *Am J Respir Crit Care Med.* 2013;188:733-748.

Sarcoidosis

- Sarcoidosis is a multisystem disorder of unknown cause(s) . It commonly affects young and middle-aged adults and frequently presents with bilateral hilar lymphadenopathy, pulmonary infiltration, and ocular and skin lesions. The liver, spleen, lymph nodes, salivary glands, heart, nervous system, muscles, bones, and other organs may also be involved.

- The diagnosis is established when clinicoradiological findings are supported by histological evidence of noncaseating epithelioid cell granulomas. Granulomas of known causes and local sarcoid reactions must be excluded.

Sarcoidosis

- The disease shows a consistent predilection for adults less than 40 yr of age, peaking in those 20 to 29 yr old . There is a second peak incidence in women more than 50 yr of age .

- annual incidence rate in the United States is 35.5 per 100,000 for blacks and 10.9 per 100,000 for whites

- the cause(s) of sarcoidosis remain unknown

Pathology- sarcoidosis

- The characteristic lesion of sarcoidosis is a discrete, compact, noncaseating epithelioid cell granuloma.
- The epithelioid cell granulomas consist of highly differentiated mononuclear phagocytes (epithelioid cells and giant cells) and lymphocytes.
- Giant cells may contain cytoplasmic inclusions such as asteroid bodies and Schaumann bodies.
- The central portion of the granuloma consists of predominantly CD4+ lymphocytes, whereas CD8+ lymphocytes are present in the peripheral zone .
- Sarcoid granulomas may develop fibrotic changes that usually begin at the periphery and travel centrally, ending with complete fibrosis and/or hyalinization .

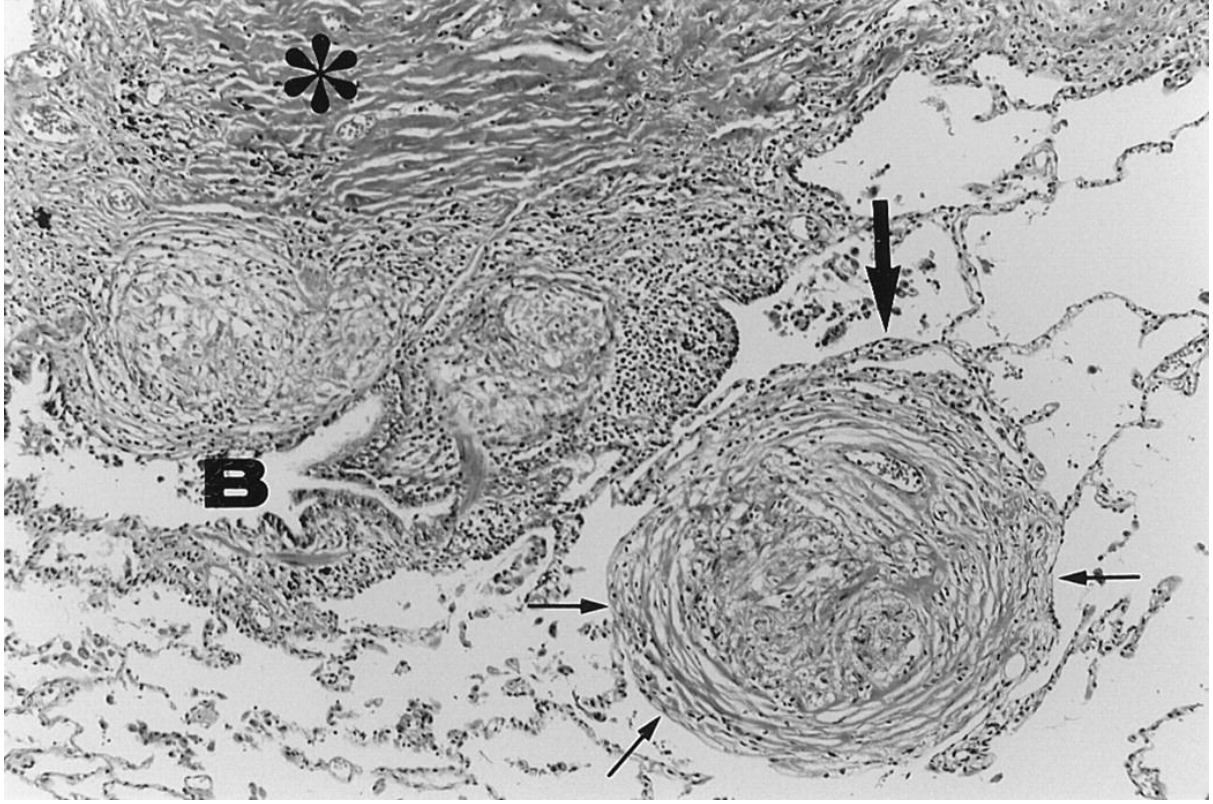


Fig. 1. Pulmonary sarcoidosis usually shows nonnecrotizing epithelioid cell granulomas predominantly in the interstitium, such as in the subepithelial layer of a bronchiole (*B*), the peribronchiolar connective tissues, and the alveolar interstitium. Sarcoid granulomas tend to undergo perigranulomatous fibrotic changes (*thin arrow*) and are sometimes replaced by hyalinous changes (*asterisk*) in the chronic stage. Alveolar septa away from the granulomas are essentially normal, except for perigranulomatous alveolar septa, which may show interstitial infiltration mainly of lymphocytes (*thick arrow*). (Surgical lung biopsy; H&E stain; original magnification, × 25.)

Am J Respir Crit Care Med,
http://www.atsjournals.org/doi/abs/10.1164/ajrccm.160.2.ats4-99

Am J Respir Crit Care Med **1999,** 160, 736-755.
DOI: 10.1164/ajrccm.160.2.ats4-99

Location and distribution

- Lymph nodes (especially intrathoracic), lungs, liver, spleen, and skin are common sites of sarcoid granulomas.

- Sarcoid granulomas either resolve or leave behind fibrotic changes. End-stage sarcoidosis causes parenchymal fibrosis and honey-combing of the lung.

Diagnosis of pulmonary sarcoidosis

- The morphologic diagnosis of pulmonary sarcoidosis relies on three main findings:

- the presence of tight, well-formed granulomas and a rim of lymphocytes and fibroblasts in the outer margin of granulomas;

- perilymphatic interstitial distribution of granulomas (which allows transbronchial biopsies to be used as sensitive diagnostic tools);
- and exclusion of an alternative cause

Clinical presentation

- *Lungs*. The lungs are affected in more than 90% of patients with sarcoidosis. Dyspnea, dry cough, and chest pain occur in one-third to one-half of all patients.

- There are five roentgenographic stages of intrathoracic changes
- Stage 0 describes no visible intrathoracic findings.
- Stage I is bilateral hilar lymphadenopathy, which may be accompanied by paratracheal adenopathy. Although lung fields are clear of infiltrates, parenchymal granulomas are often found in lung tissue biopsies.
- Stage II is bilateral hilar adenopathy accompanied by parenchymal infiltration.
- Stage III is parenchymal infiltration without hilar adenopathy.
- Stage IV consists of advanced fibrosis with evidence of honey-combing, hilar retraction, bullae, cysts, and emphysema.

CHEST RADIOGRAPHIC STAGING

stage		frekvence
0	Normal chest radiograph	5-10%
I	Bilateral hilar lymphadenopathy (BHL)	50%
II	BHL plus pulmonary infiltrations	25%
III	Pulmonary infiltrations (without BHL)	15%
IV	Pulmonary fibrosis	5-10%

Classification is based on the posteroanterior chest radiogram only. Sometimes a CT scan

Organ Involvement- sarcoidosis

organ	% patients
mediastinal lymph nodes	95-98%
lung	90 %
liver	50-80%
splen	40-80%
eye	20-50%
periferní lymfatické uzliny	30%
skin	25%
nervous system	10%
heart	5%

Costabel.U. Sarcoidosis: clinical update, ERJ July 1, 2001 vol. 18 no. 32 suppl 56s-68s

RECOMMENDED INITIAL EVALUATION OF PATIENTS WITH SARCOIDOSIS

- 1.History (occupational and environmental exposure, symptoms)
- 2.Physical examination
- 3.Posteroanterior chest radiography
- 4.Pulmonary function tests: spirometry and DLCO
- 5.Peripheral blood counts: White blood cells, red blood cells, platelets
- 6.Serum chemistries: calcium, liver enzymes (alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase), creatinine, BUN
- 7.Urine analysis
- 8.ECG
- 9.Routine ophthalmologic examination
- 10.Tuberculin skin test

Definition of abbreviations: BUN = blood urea nitrogen; DL CO = diffusing capacity of the lung for CO; ECG = electrocardiogram.

Costabel.U. Sarcoidosis: clinical update, ERJ July 1, 2001 vol. 18 no. 32 suppl 56s-68s

Lung CT scan

(*1*) widespread small nodules with a bronchovascular and subpleural distribution,

(*2*) thickened interlobular septae,

(*3*) architectural distortion,

(*4*) conglomerate masses.

- Less common findings are: (*1*) honeycombing, (*2*) cyst formation and bronchiectasis, and (*3*) alveolar consolidation

Natural history

- spontaneous remissions occur in nearly two-thirds of patients, but the course is chronic or progressive in 10 to 30%

- one-third to one-half of patients with sarcoidosis were treated with corticosteroids

Treatment

- In patients with systemic, symptomatic disease, oral corticosteroids are often employed. Systemic therapy is clearly indicated for cardiac disease, neurologic disease, eye disease not responding to topical therapy, and hypercalcemia.
- Methotrexate, azathioprine
- Lung and other organ transplantation has been successfully performed for patients with end-stage sarcoidosis