Interstitial Lung Diseases

Pavol Joppa, MD, PhD

Dept. of Pneumology and Phthisiology

Diffuse interstitial lung disorders

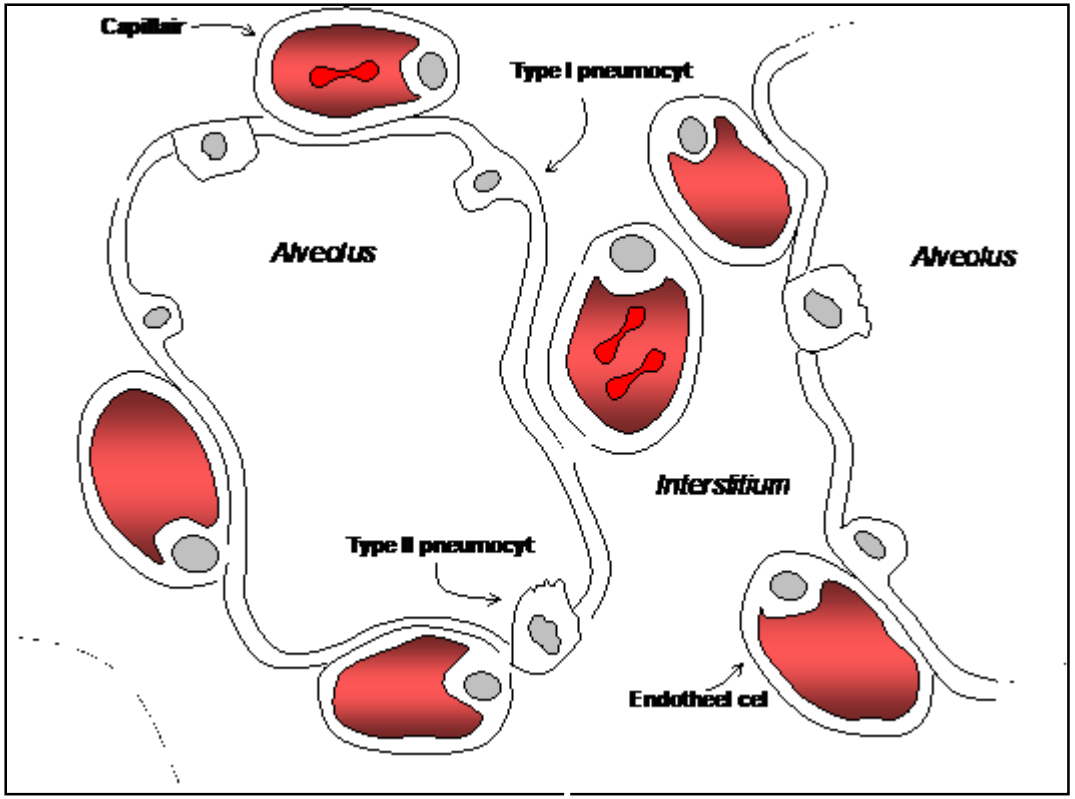
(~ 200 nosological entities)

- Hamman and Rich - 1935 – the first description of a rapidly progressive variant
-
- In all interstitial disorders:
  1. Inflammatory infiltrate in aveoli - **alveolitis**
  2. Concomitant fibrotic changes in the interstitium - **fibrosis**

PATHOGENESIS

Varying patterns of **inflammation** and **fibrosis**

Environmental factors



Without known causes or associations

Host genetic factors

IDIOPATHIC

- idiopathic interstitial pneumonias - IIP

SECONDARY

a) Disorders with known etiology

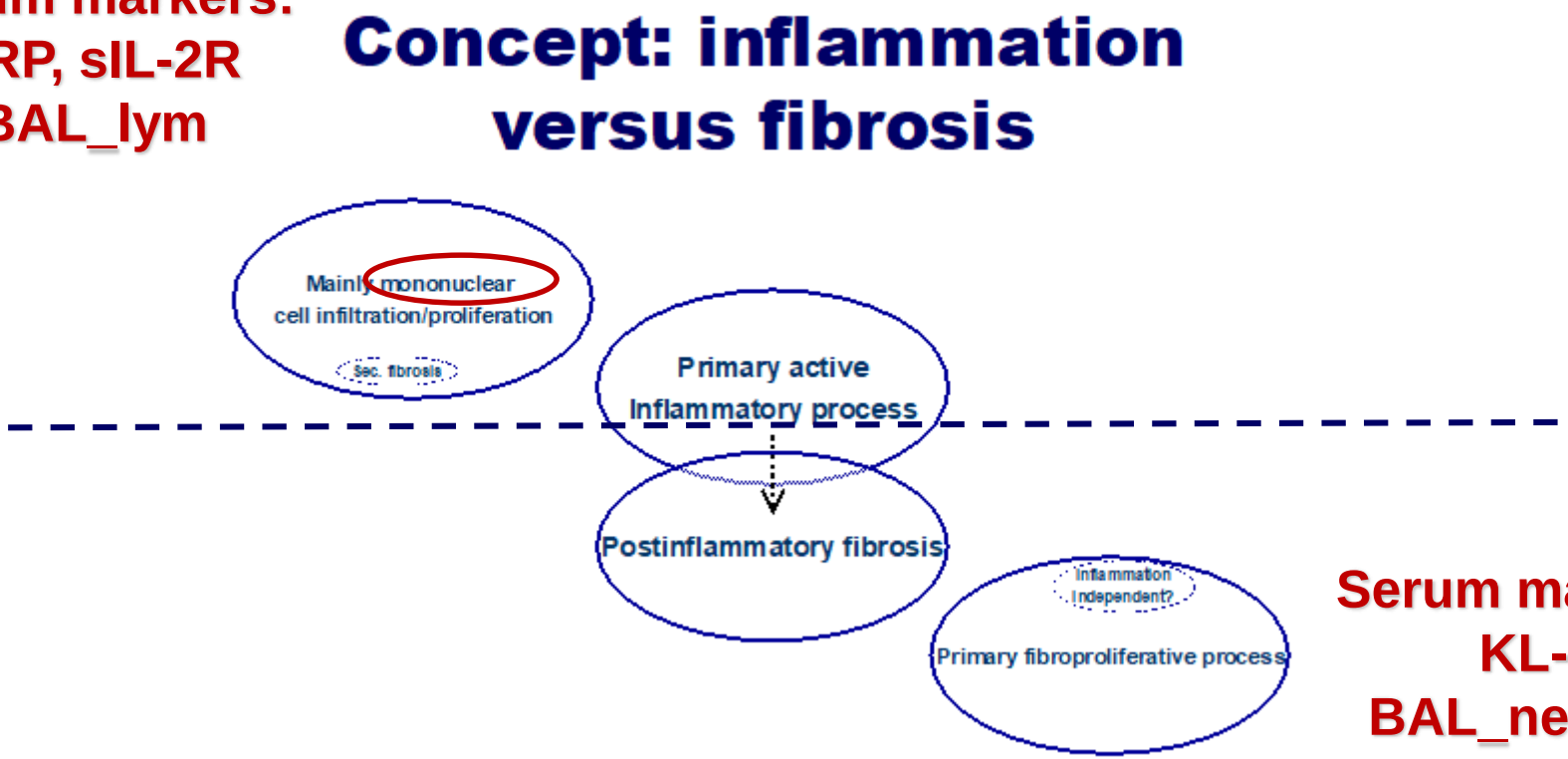
- **pneumoconioses**
- hypersensitivity pneumonitis (EAA)
- drugs – **bleomycine, cordarone**
- ARDS
- c**arcinomatous** lymfangiopathy
- post-irradiation fibrosis

b) Disorders with unknown etiology

- systemic connective tissue diseases - **progressive systemic sclerosis, lupus, rheumatoid arthritis**
- **sarcoidosis**
- vasculitis –**granulomatosis with angiitis (Wegener)**

Between IIPs there are large differences in the role of inflammatory and fibrotic processes

Serum markers:
CRP, sIL-2R
BAL_lym



Serum markers:
KL-6
BAL_neu/eos

7 histological categories of IIP

- Usual interstitial pneumonia (UIP)
- Nonspecific interstitial pneumonia (NSIP)
- Cryptogenic organising pneumonia (COP)
- Diffuse alveolar damage (DAD – Acute IP)
- Desquamative interstitial pneumonia (DIP)
- Respiratory bronchiolitis (RB-ILD)
- Lymphocytic interstitial pneumonia (LIP)

Idiopathic pulmonary fibrosis (IPF)

- Histological pattern: Usual interstitial pneumonia (UIP)
- Clinically isolated lung involvement, secondary causes ruled out (i.e. systemic connective tissue disease)
- Radiologically typical features in CT scans

Diagnostic procedures

- **History:** exposition (professional or nonprofessional)
  drugs

- **Symptoms***:* *common*
  nonproductive irritating cough
  dyspnoea (physical exercise)
  hemoptyses

  less common
  pleural pain, retrosternal pain
  myalgia, arthralgia, joint oedema
  weight loss
  increased temperature, fever

Diagnostic procedures

- **Auscultation: Dry crepitations** – lung bases, bilaterally

(„velcro“ – phenomena)

- Pulmonary hypertension, cor pulmonale
- **Symptoms of right ventricular failure**
- Cyanosis

Diagnostic procedures

Pulmonary function tests

- **Restrictive ventilatory pattern – reduction in all volumes (FEV1, FVC, TLC, RV...)**
- **FEV1/FVC ratio – normal, *i.e.* >0.70**
- Reduction in inspiratory reserve volume is the most pronounced phenomenon

- Lung diffusion capacity reduced – **DLCO !**

Diagnostic procedures

Laboratory

- Auto-antibodies
- antinuclear Abs (ANA), rheumatoid factor, Abs against cytoplasm of neutrophils (ANCA), against glomerular basal membrane, etc....

Autoantibody	Rheumatoid arthritis	Systemic lupus erythematosus	Sjögren's syndrome	PSS (scleroderma)	Polymyositis/ dermatomyositis
Rheumatoid factor	Common*	Common	Common	Common	Rare†
Antinuclear antibody	Common	Common	Common	Common	Rare
Double- stranded DNA (ds- DNA)	Undetectable	Diagnostic	Undetectable	Undetectable	Undetectable
Smith (Sm) antibody	Undetectable	Diagnostic	Undetectable	Undetectable	Undetectable
Ro(SSA)/La(SSB) ("Sjögren's antibodies")	Uncommon‡ (associated with Sjögren's)	Uncommon (associated with Sjögren's)	Common	Uncommon	Rare
Centromere	Undetectable	Undetectable	Rare	Common in limited PSS	Rare
SCL- 70 (topoisomerase 1)	Undetectable	Undetectable	Rare	Common in diffuse PSS	Rare
Jo- 1 (synthetase)	Undetectable	Undetectable	Undetectable	Rare	Common in patients with interstitial lung disease
Antineutrophil cytoplasmic antibody (ANCA)	Rare	Rare	Uncommon	Undetectable	Uncommon

> 25% of patients† < 5% of patients‡ 5%–25% of patients PSS—progressive systemic sclerosis.

Diagnostic procedures

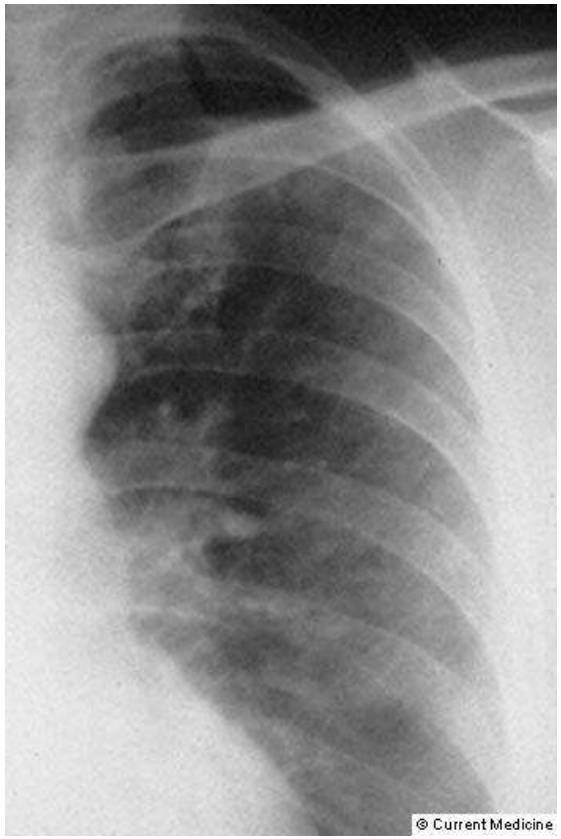
X-Ray

- bilateral, mostly symmetrically disseminated micronodular, reticular or reticulo-nodular infiltrations

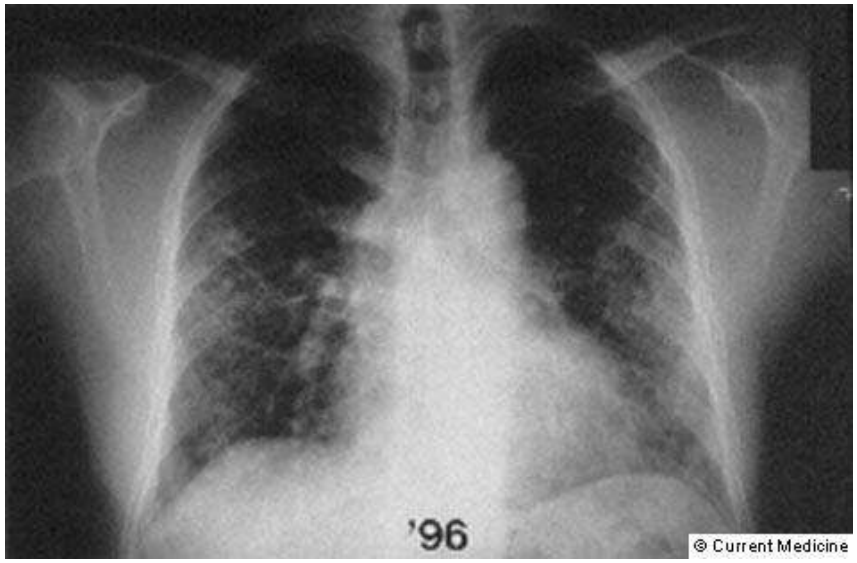
- ground-glass appearance (alveolitis)

- honey-comb lung (fibrosis)

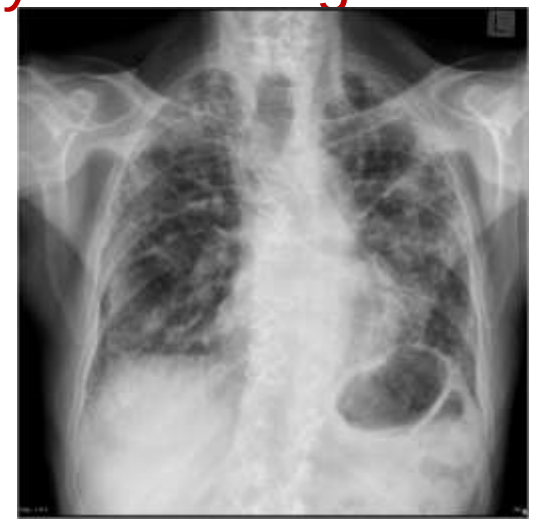
micronodular, reticular or reticulo-nodular infiltrations



ground-glass appearance
alveolitis



honey-comb lung - **fibrosis**

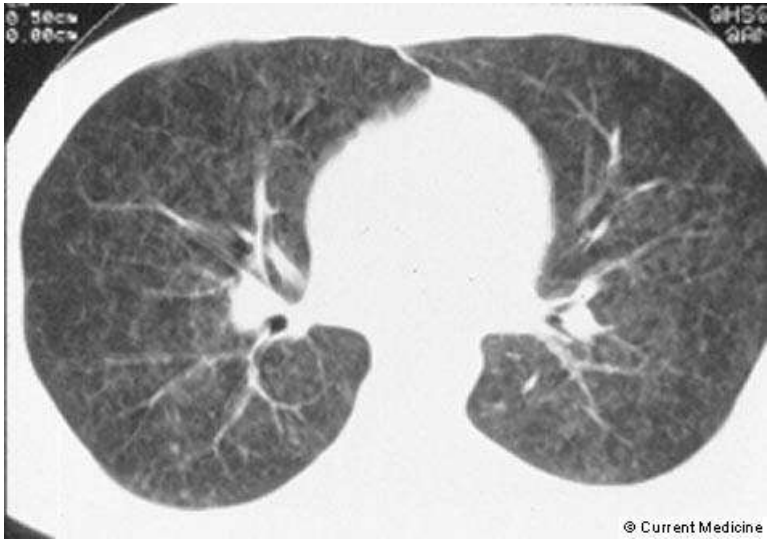


Diagnostic procedures

HRCT

ground-glass appearance

alveolitis



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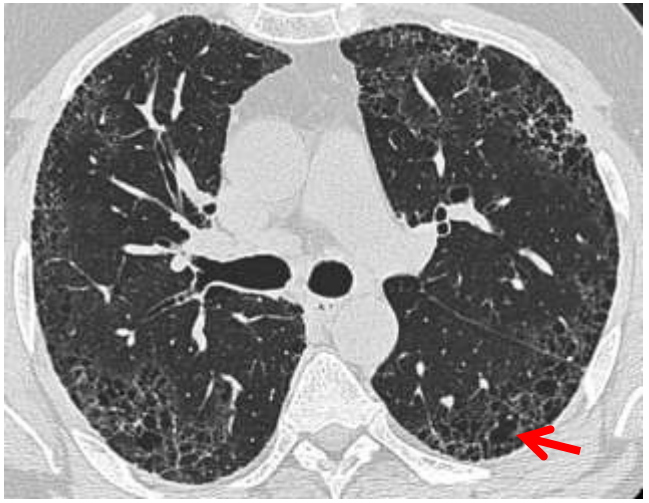
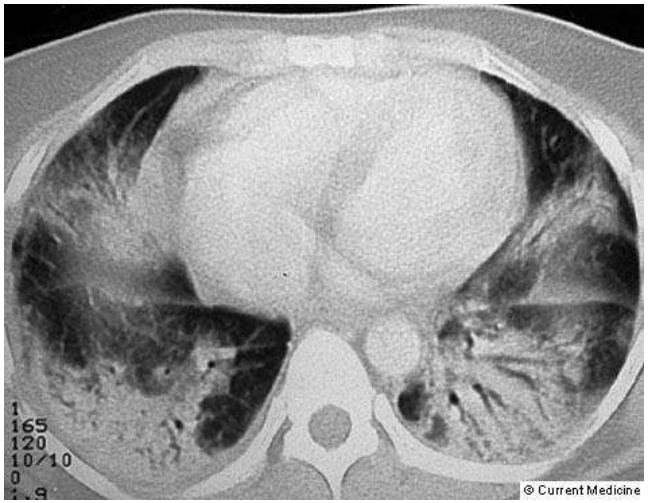




Diagnostic procedures

- **Bronchoscopy**
- **+ Bronchoalveolar lavage** (type of cells – flow cytometry)

- **Biopsy –** open lung biopsy (rare)
  - video-assisted thoracoscopy (VATS)
  - transbronchial biopsy (in some cases)

Diagnostic procedures

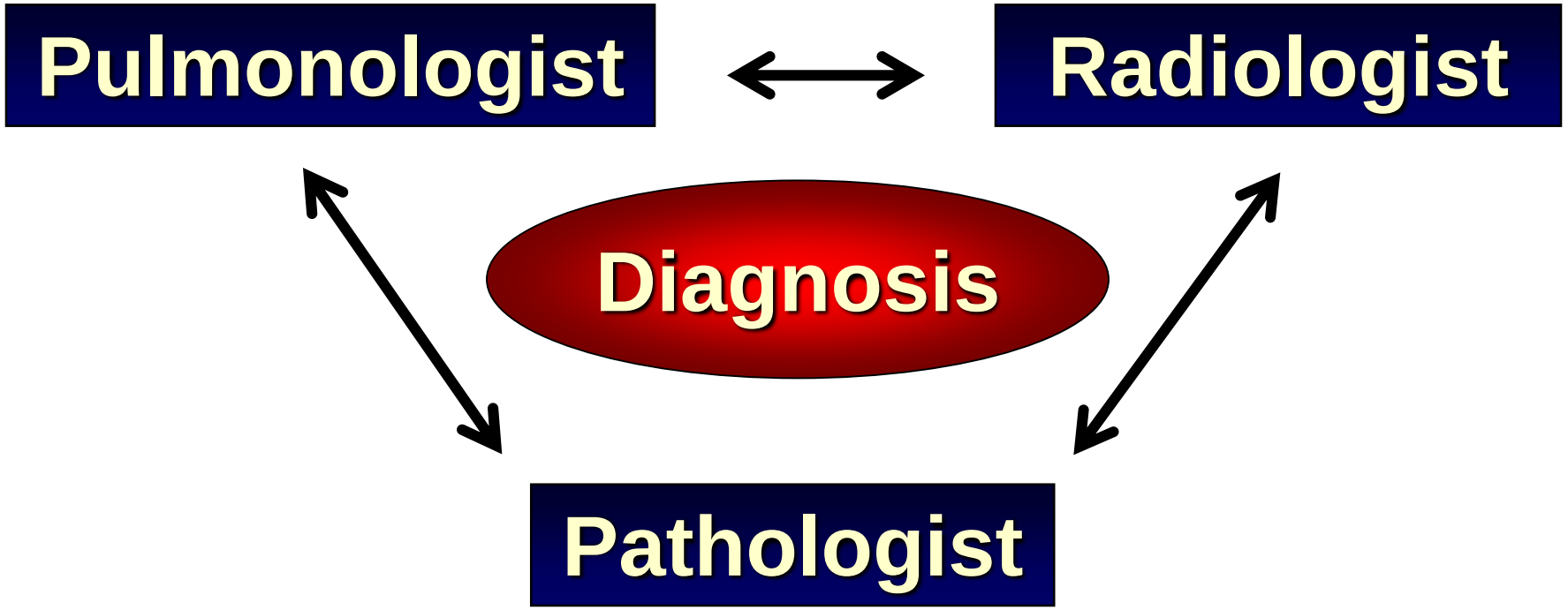
Arterial blood gases

a) Initially – hypoxaemia (on exertion), hyperventilation (hypocapnia)

partial – hypoxaemic respiratory failure

b) Progressive disease: hypoxaemia + hypercapnia

global respiratory failure



Correct IIP diagnoses need teamwork and experience

Therapy - IIP

- Systemic steroids**:** Prednisone

  Pulse corticotherapy - metylprednisolone
- Immunosuppressive therapy: Azathioprine

  Cyclophosphamid

- Antifibrotic therapy (NEW - specific **for IPF – idiopathic pulmonary fibrosis**) PIRFENIDONE

  NINTEDANIB (tyrosine-kinase inhibitor)

- **Long term home oxygen therapy (LTOT)**
- Lung transplantation

Sarcoidosis

Morbus Boeck-Besnier-Schaumann

Multisystemic **granulomatous** disorder (myocardium, central nervous system, eye)

Thoracic sarcoidosis

Stage 1: lymph nodes

Stage 2: lymph nodes + lung parenchyma

Stage 3: lung parenchyma

Stage 4: fibrosis

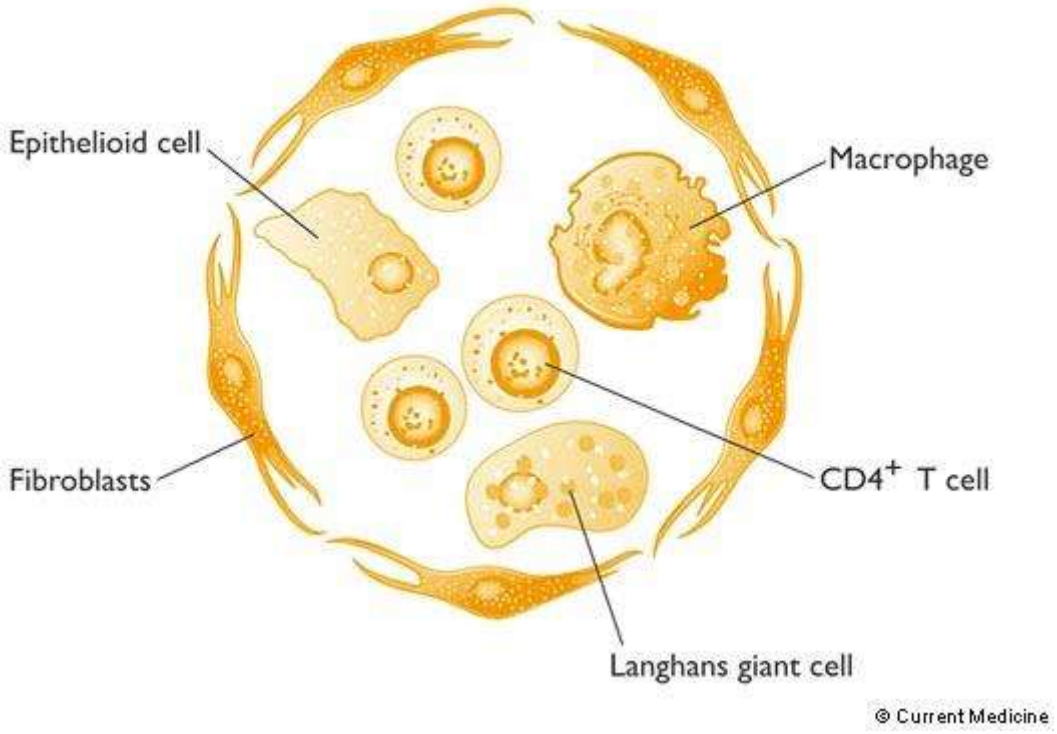


Figure Contents of the sarcoid granuloma. The center of the granuloma frequently contains lymphocytes, macrophages, epithelioid cells, and foreign body and/or Langhans giant cells.
They are frequently surrounded by a rim of fibrosis, with fibroblastic cells that elaborate collagen.

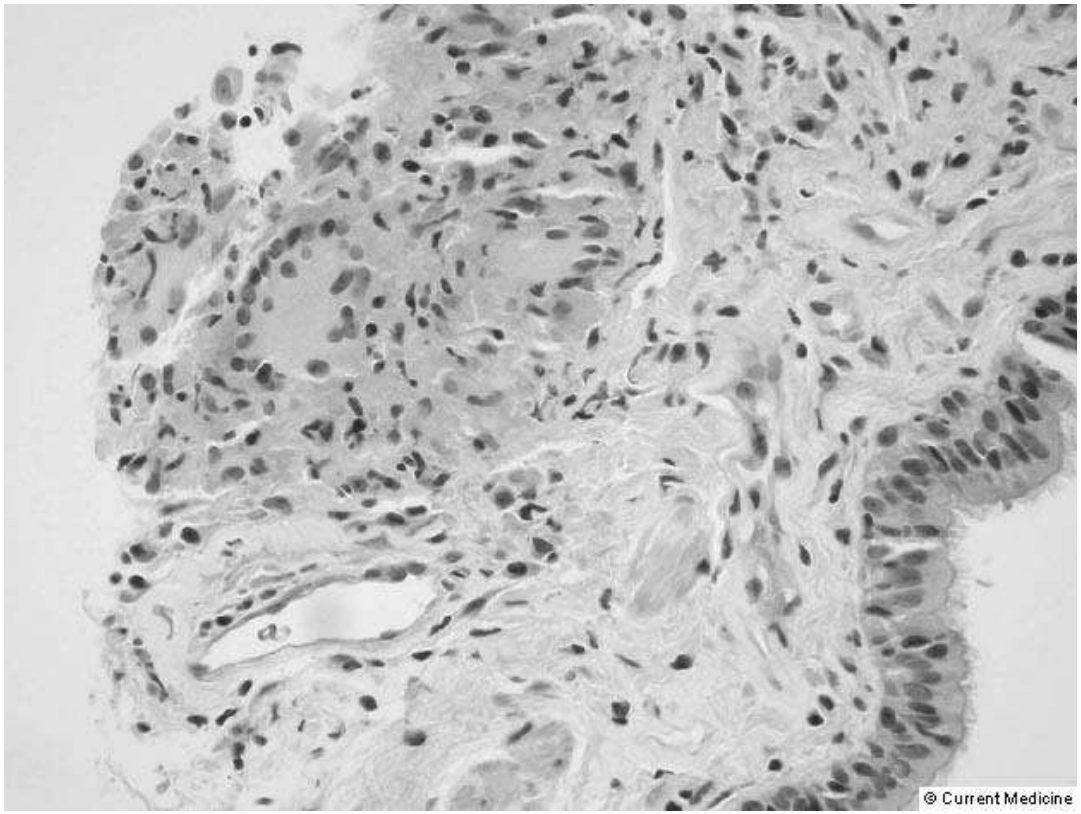
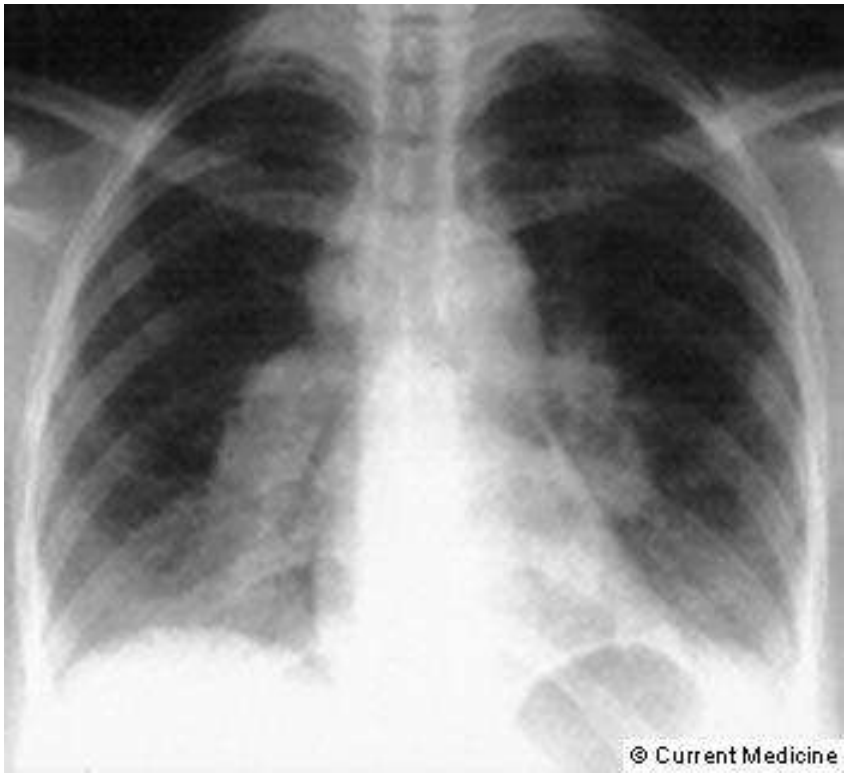
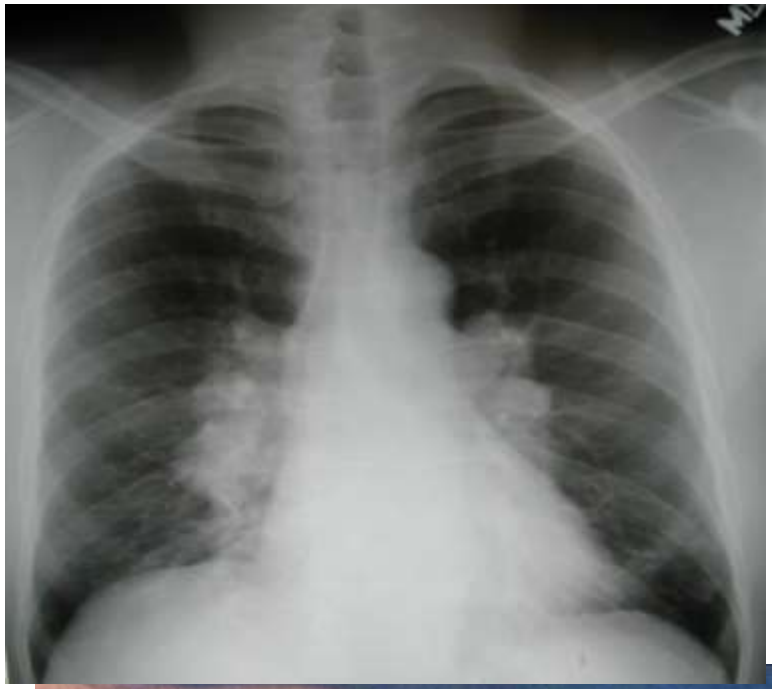


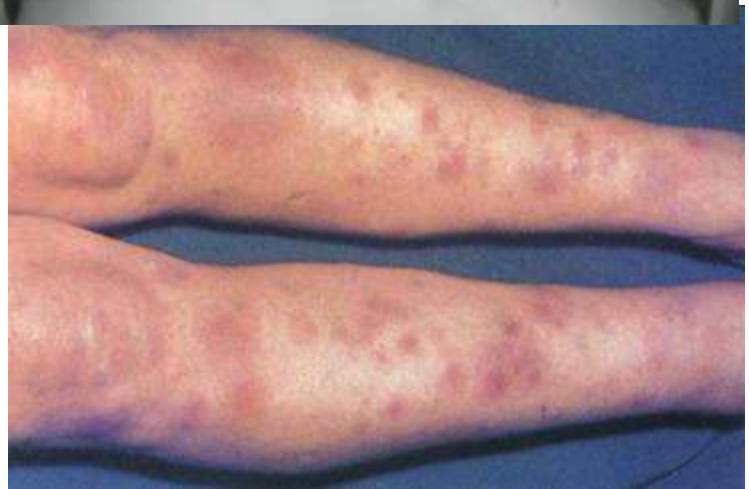
Figure 12-3. Transbronchial lung biopsy taken from a patient with pulmonary sarcoidosis. The photomicrograph demonstrates a granuloma with a prominent central **multinucleated giant cell**, adjacent to respiratory epithelium. There is **no evidence of caseation**. The location of granuloma in peribronchial tissue is a typical feature of sarcoidosis and contributes to the high diagnostic yield of bronchoscopic biopsy.



Chest radiograph of a patient with stage I sarcoidosis.

Löfgren's syndrome



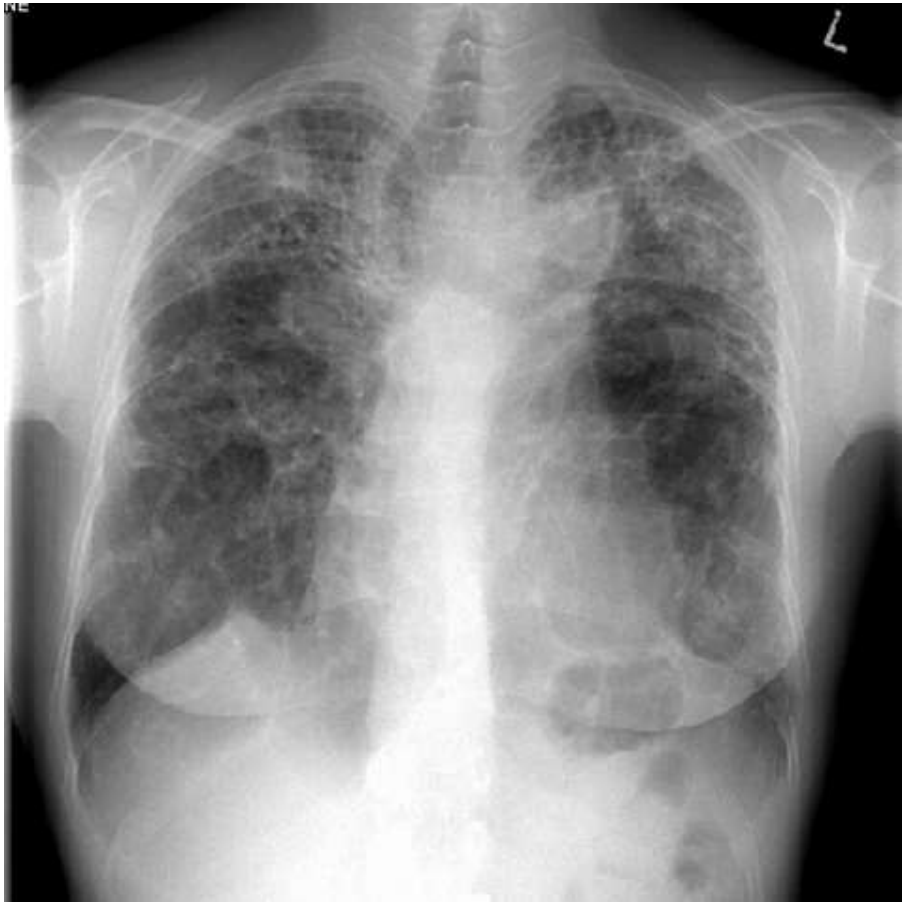


- **acute onset with fever**
- **erythema nodosum**
- **bilateral hilar lymphadenopathy**
- **joint symptoms / arthritis**
- **good prognosis**

Differential Diagnosis of Stage I Sarcoidosis

- Infection
  - Mycobacteria (tuberculosis, atypical mycobacteria)
  - Fungal infection
  - Viral infection (HIV, mononucleosis)
- Malignancy
  - Lymphoma
  - Metastatic disease
- Inflammation/other
  - Berylliosis
  - Pulmonary hypertension

Stage 3 sarcoidosis (global sarcoid)



Therapy

Only progressive forms

Pulmonary fibrosis with reduction in VC and diffusing capacity

Affection of vital organs (myocardium, eye...)

Hypercalciuria with renal impairment

Systemic corticosteroids - Prednisone