

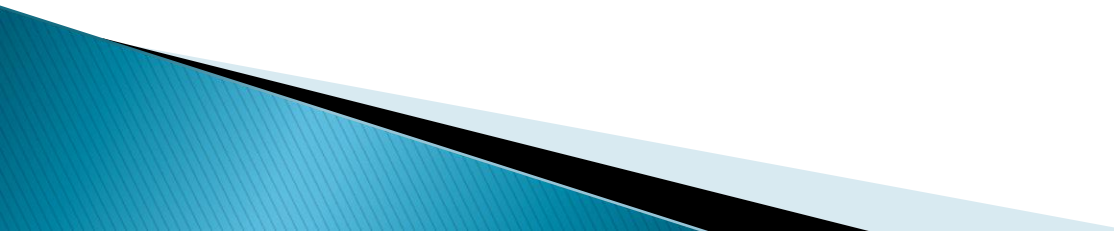


*Good
morning
everyone ~
and welcome!*

PULMONARY MANIFESTATIONS OF COLLAGEN VASCULAR DISEASES

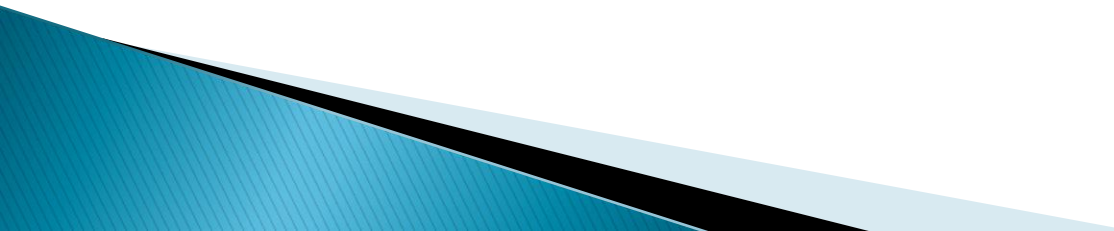
Dr Romi Singla

RHEUMATOID ARTHRITIS

- ▶ Pleuropulmonary complications 50% incidence.
 - ▶ More in patients with more severe chronic articular disease, with high titers of RA factor, patients with subcutaneous nodules plus other systemic complications s.a. cutaneous vasculitis, myocarditis, pericarditis, ocular inflammation, Felty's Syndrome.
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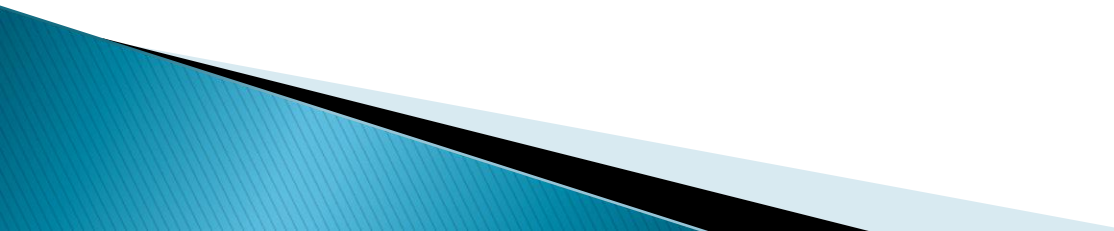
- ▶ Association between Smoking and the risk for the development of pleuropulmonary disease.
- ▶ May precede the articular manifestations by months to years.

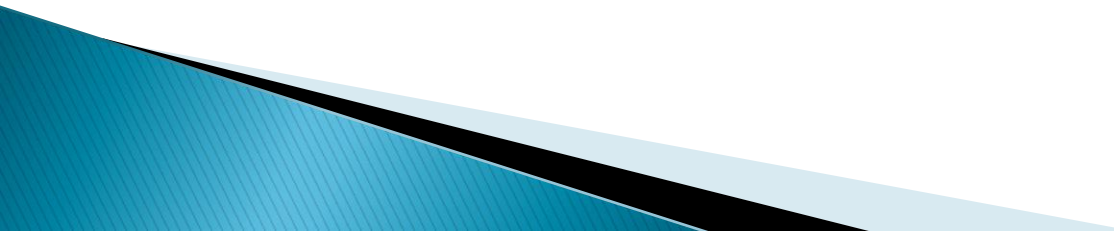
Pulmonary manifestations are:

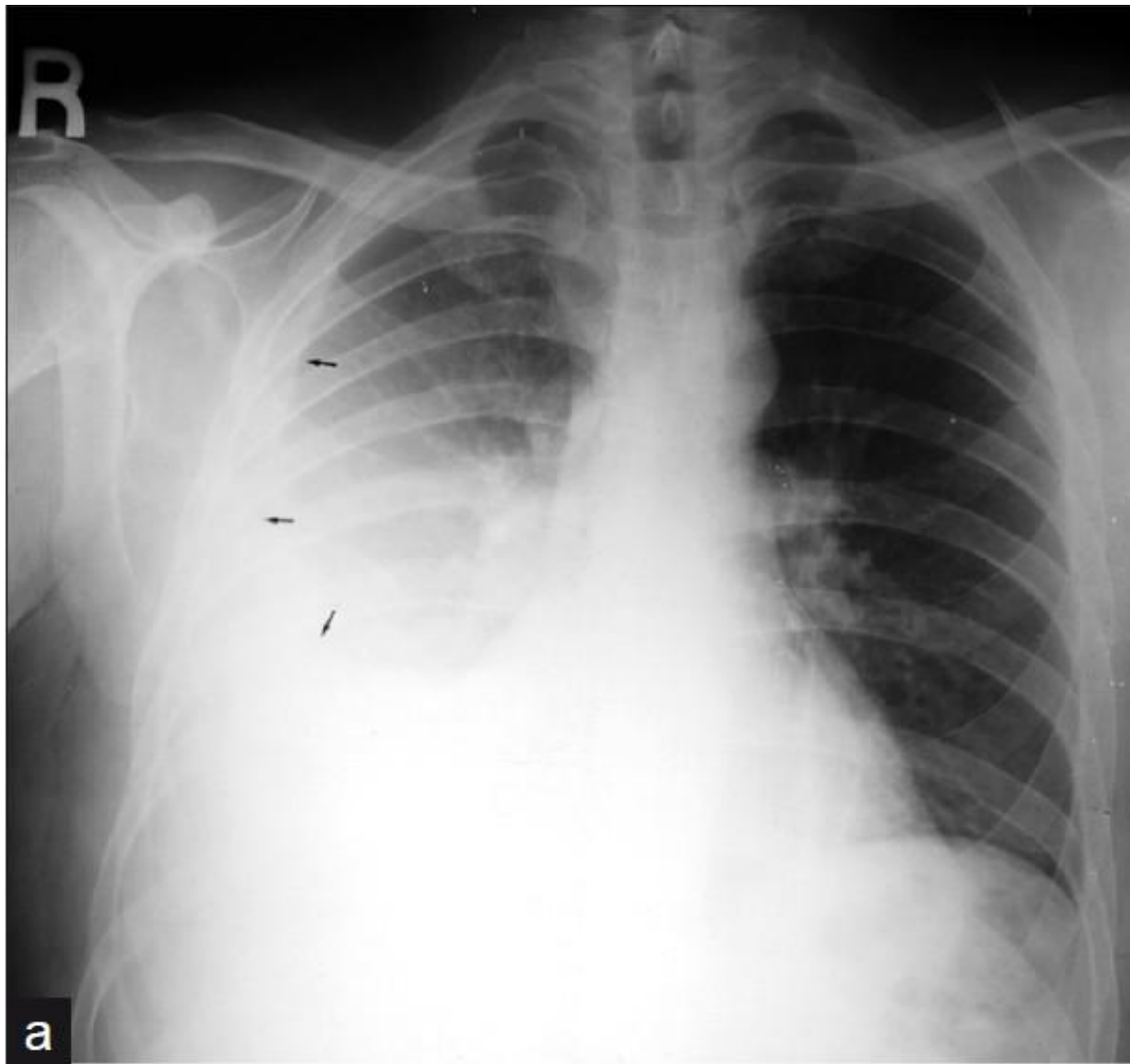
- ▶ Pleurisy and Pleural Effusion
 - ▶ Pulmonary Vascular disease
 - ▶ Necrobiotic (Rheumatoid) Nodule
 - ▶ Airway Disease
 - ▶ Interstitial Lung Disease
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Pleurisy and Pleural effusion

- ▶ Postmortem series 40%
- ▶ Clinically apparent 5%
- ▶ More common in men
- ▶ Most frequently during episodes of Active articular disease and subcutaneous rheumatoid nodules.

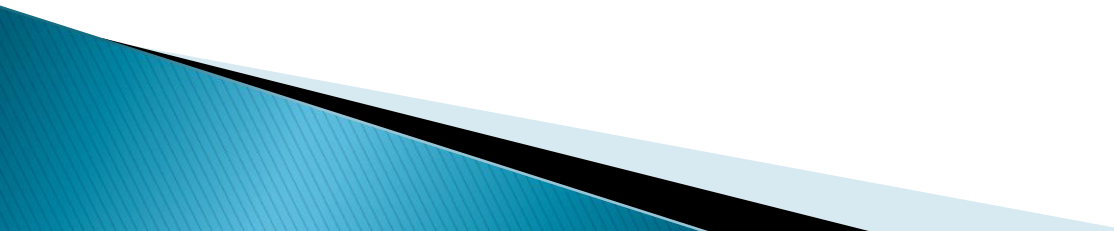
- ▶ U/L or B/L
 - ▶ Symptoms: Pleuritic pain and Dyspnea
 - ▶ Fever +/–
 - ▶ Exudate
 - ▶ Increased Cholesterol conc. In chronic disease
 - ▶ Low pH < 7.2
 - ▶ TLC may be 15,000/cumm
 - ▶ Complement low
 - ▶ RA factor increased
- 

- ▶ Low pleural fluid Glucose conc.
 - ▶ 75% have $<50\text{mg\%}$
 - ▶ Cytology: Spindle shaped macrophages, necrotic debris, multinucleated histiocytes
 - ▶ Asymptomatic cases No Treatment
 - ▶ Corticosteroids
 - ▶ Pleural fibrosis with lung entrapment – Surgery
 - ▶ Spontaneous pneumothorax d/t ruptured necrobiotic nodule – Tube thoracostomy
 - ▶ Persistence of BPF – Surgery
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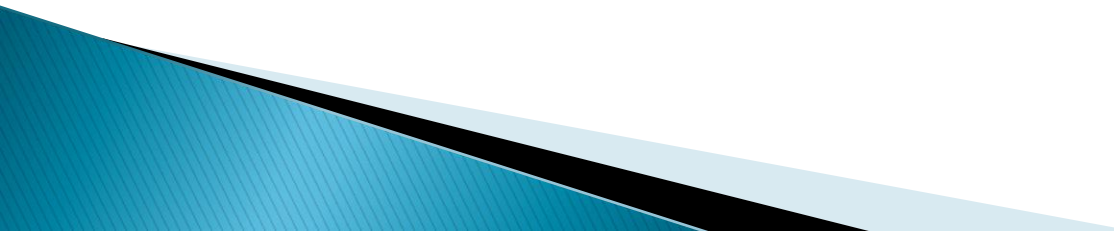
A 52-year-old male with rheumatoid arthritis (RA): (a) PA chest radiograph shows a moderate right sided pleural effusion (arrow)

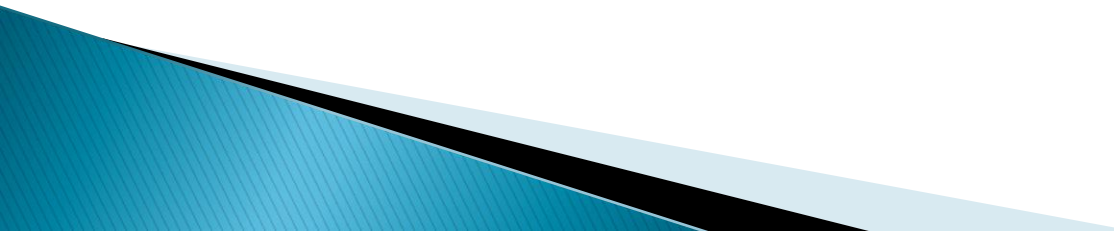
Pulmonary Vascular Disease

- ▶ Least common
 - ▶ Fibroproliferative plexogenic arteriopathy infrequent
 - ▶ Raynaud's phenomenon common
 - ▶ CXR – normal lung fields, enlarged pulmonary arteries
 - ▶ Isolated reduction of DLCO, Hypoxemia
- 

- ▶ Small vessel vasculitis in the setting of Diffuse Alveolar haemorrhage (DAH) d/t pulmonary capillaritis – very rare.
- ▶ Treatment – i/v methylprednisolone, Oral corticosteroids, cyclophosphamide

Necrobiotic (Rheumatoid) nodule

- ▶ Infrequent <1%
 - ▶ More common on men, smokers
 - ▶ With active articular disease
 - ▶ High RA Factor
 - ▶ Have subcutaneous nodules
 - ▶ Most are Asymptomatic
 - ▶ Occasionally, cough and hemoptysis
- 

- ▶ Single/Multiple
 - ▶ Upper and Mid zone predilection
 - ▶ 50% undergo cavitation
 - ▶ Upto 7 cm
 - ▶ Spontaneous resolution
 - ▶ Recurrence
 - ▶ Continuous growth, aggressive diagnostic approach
 - ▶ Most cases, No Treatment.
- 

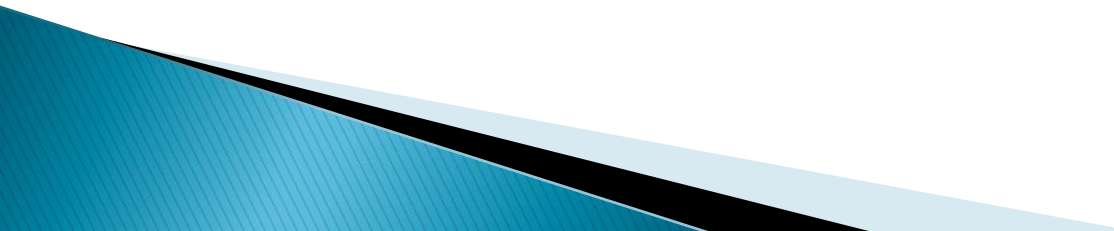
CAPLAN'S SYNDROME:

- ▶ Welsh coal miners 1953
- ▶ Discrete nodules
- ▶ Upper lobes
- ▶ Histologically identical to Necrobiotic nodule
- ▶ Peripheral, well-defined, solitary or multiple nodules often appear rapidly in crops at times of increased rheumatoid arthritis activity and are often associated with new subcutaneous nodules.
- ▶ Biopsy reveals inorganic dust within the necrotic nodule.
- ▶ The nodules are asymptomatic and do not require treatment unless a complication develops following rupture of a cavitating lesion into the pleural space.
- ▶ Higher incidence with underlying pneumoconiosis, CWP, Silicosis, Asbestosis

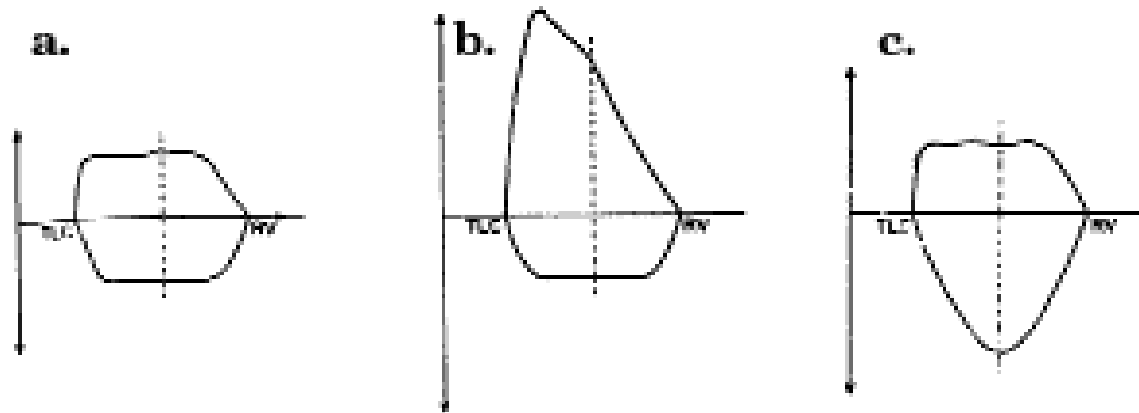


A 57-year-old male (ex-miner): A frontal chest radiograph shows Caplan's syndrome.

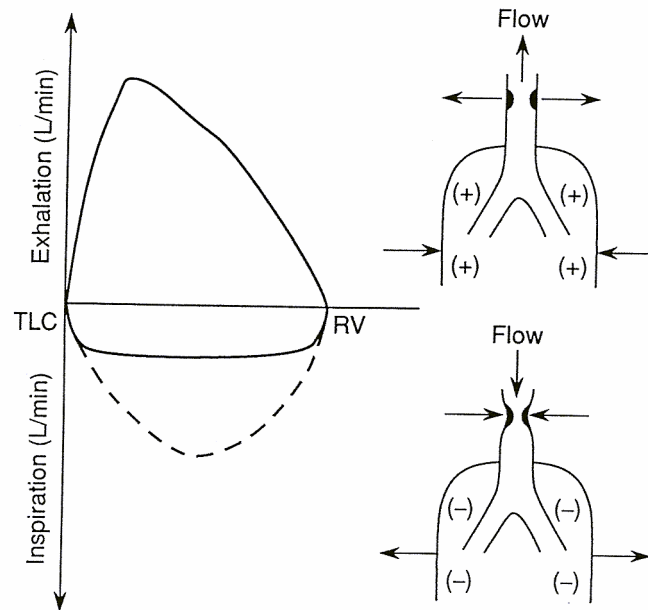
Airway Disease

- ▶ No other CVD involves airways as much as RA.
 - ▶ Cricoarytenoid joint
 - ▶ Stridor
 - ▶ Sore throat, HoV, Globus sensation
 - ▶ Prevalence 50%
 - ▶ Clinically significant disease – Flow–volume loops, variable extrathoracic obstruction of the inspiratory loop.
- 

- ▶ Cricoarytenoid arthritis complicate endotracheal intubation during GA.




*Miller and Hyatt defined Flow-volume patterns in upper-airway obstruction. The dotted lines represent the midpoints of the maximal expiratory and inspiratory flows. a. Fixed upper-airway obstruction (intrathoracic or extrathoracic). **b. Variable extrathoracic obstruction.** c. Variable intrathoracic obstruction.*

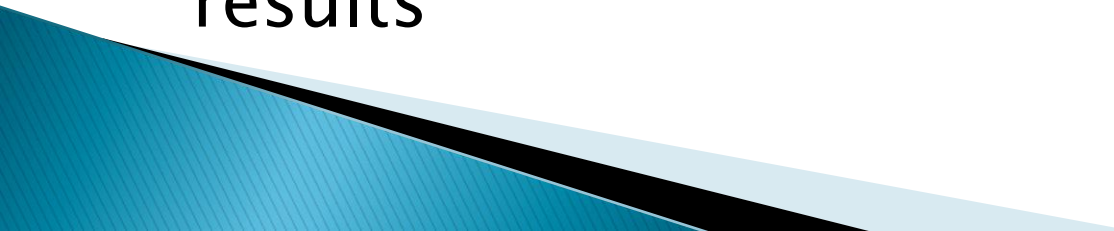


Schematic representation of an extrathoracic variable obstruction. The solid lines represent actual curves, while the dashed line represents a normal inspiratory pattern. Note that with the extrathoracic variable obstruction, exhalation induces a positive intratracheal pressure, which in turn results in little or not resistance to flow past the narrowed segment (top figure). Conversely, inhalation generates negative intrathoracic pressure, which in turn induces negative pressure in the trachea below the point of obstruction. This negative pressure will induce further obstruction and increase resistance to flow

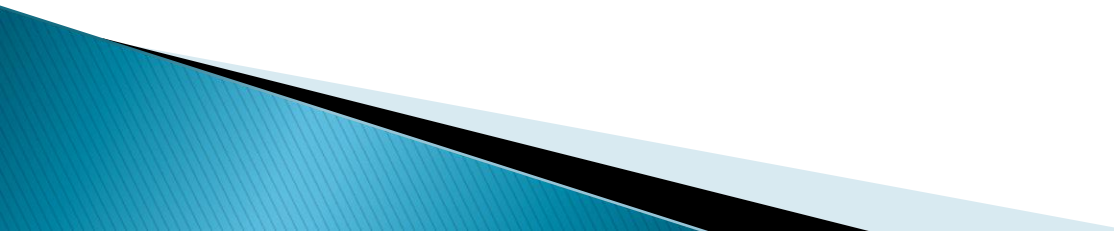
BRONCHIOLITIS OBLITERANS:

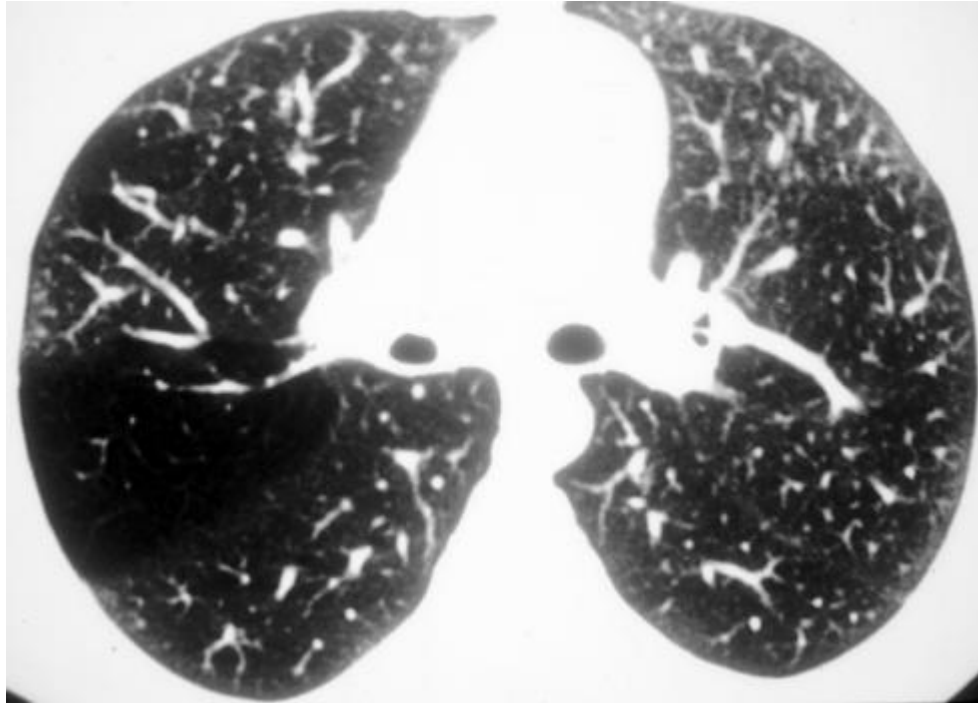
- ▶ Obstructive lung disease
 - ▶ Insidious onset
 - ▶ Progressive dyspnea and cough
 - ▶ Normal or Hyperinflated CXR
 - ▶ P/E: Reduced breath sounds, occasionally an inspiratory squeak
 - ▶ PFTs: Airflow limitation, reduced/ normal diffusing capacity
 - ▶ HRCT : Adjacent areas of decreased and increased attenuation (geographic pattern) air trapping
 - ▶ Majority progress to Hypercapnic Resp. Failure.
- 

RESPIRATORY/FOLLICULAR BRONCHIOLITIS:

- ▶ A dense infiltration of lymphocytes and plasma cells surrounding the terminal and respiratory bronchioles.
 - ▶ Cough, Dyspnea
 - ▶ CXR: Normal/ fine nodular, more prominent middle and lower zones
 - ▶ HRCT: Centrilobular nodules and bronchiectasis
 - ▶ Usually no physiological evidence of airflow limitation or reduced lung volumes
 - ▶ Gas exchange abnormalities dominate
 - ▶ Treatment with corticosteroids variable results
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DIFFUSE PANBRONCHIOLITIS:

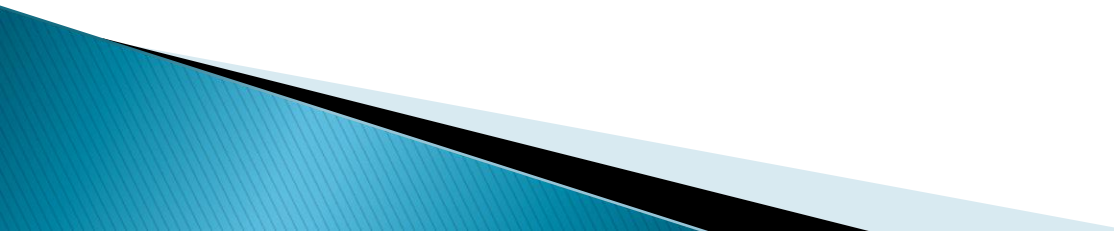
- ▶ Japanese patients with RA
 - ▶ Both Diffuse panbronchiolitis and RA, an association with HLA-DR4 and B54, suggesting a common genetic predisposition.
- 



Bronchiolitis Obliterans

Radiologically, *bronchiectasis* in rheumatoid arthritis has been described in several series and may precede the onset of rheumatoid arthritis. It may be secondary to interstitial fibrosis (traction bronchiectasis) or isolated.

On computed tomography, bronchiectasis and *bronchiolectasis* have been demonstrated in 30%



Bronchocentric granulomatosis—

This is a granulomatous inflammation of the airways, usually associated with asthma and aspergillus and, rarely, associated with rheumatoid arthritis.

Presentation is with dyspnoea, cough, haemoptysis, and chest pain.

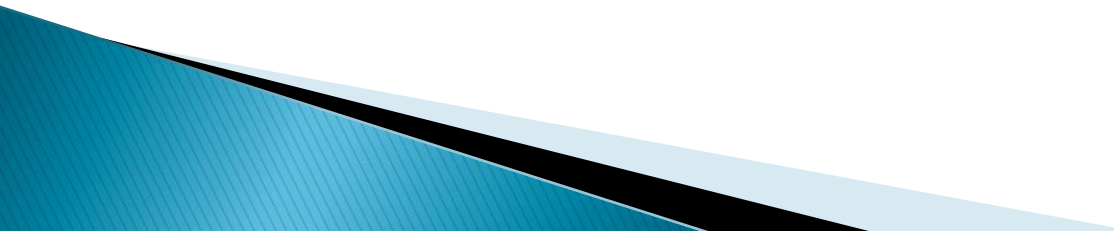
Imaging reveals unilateral or bilateral nodules, measuring several centimetres, possibly with cavitation, which are bronchocentric in distribution on computed tomography.

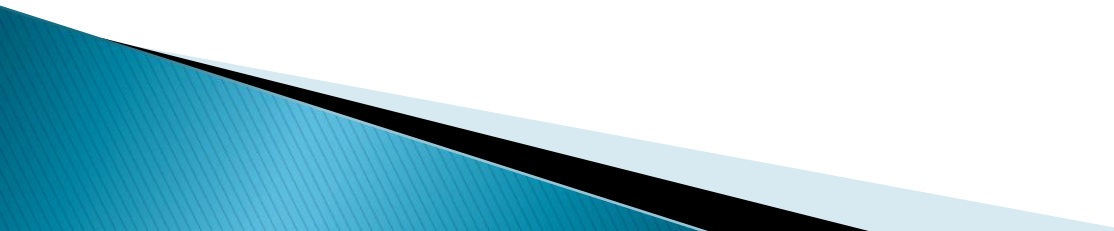
Histologically the features are similar to rheumatoid arthritis nodules.

Nodules may remain static or resolve with steroids.




Interstitial Lung Disease

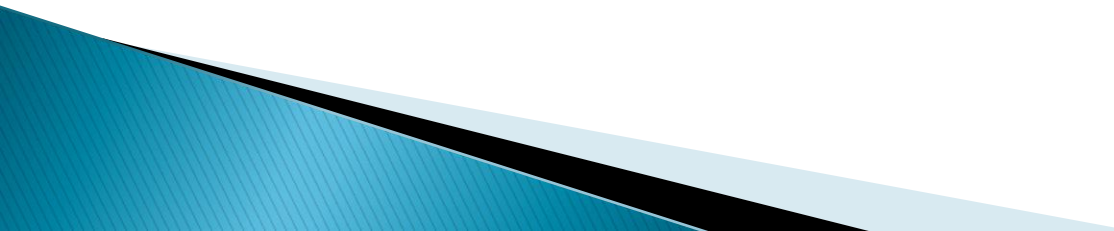
- ▶ Relatively common
 - ▶ More common in males (M:F= 3:1)
 - ▶ Who have late onset disease
 - ▶ High titer of RA factor
 - ▶ Smokers
 - ▶ Clinically important ILD in 5–10%
 - ▶ Most common UIP, and degrees of NSIP
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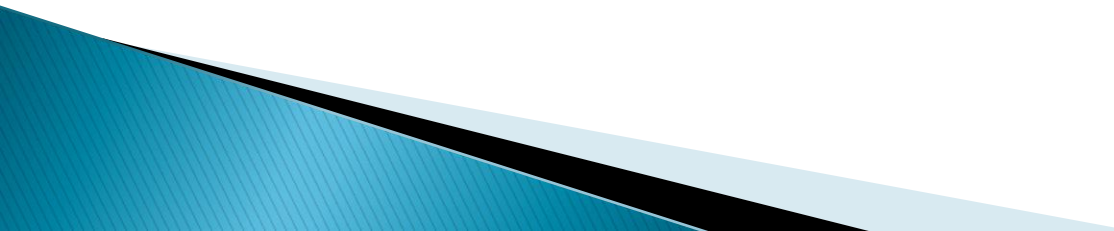
- ▶ Dyspnea, cough
 - ▶ Bibasilar crackles
 - ▶ Clubbing in 75%
 - ▶ Pulmonary hypertension
 - ▶ Cor pulmonale
 - ▶ CXR and HRCT: Interstitial infiltrates, lung bases and lung periphery
 - ▶ Ground glass attenuation, mixed alveolar interstitial infiltrates NSIP
- 

Other interstitial reactions:

- ▶ BOOP – Symptoms identical to UIP, CXR and CT differ from UIP because the infiltrates are primarily alveolar and localized, patchy, or diffuse.
 - ▶ LIP – When RA is complicated by Sjogren's Syndrome. CXR patchy alveolar infiltrates primarily at the lung bases.
 - ▶ Eosinophilic Pneumonia – Recently reported.
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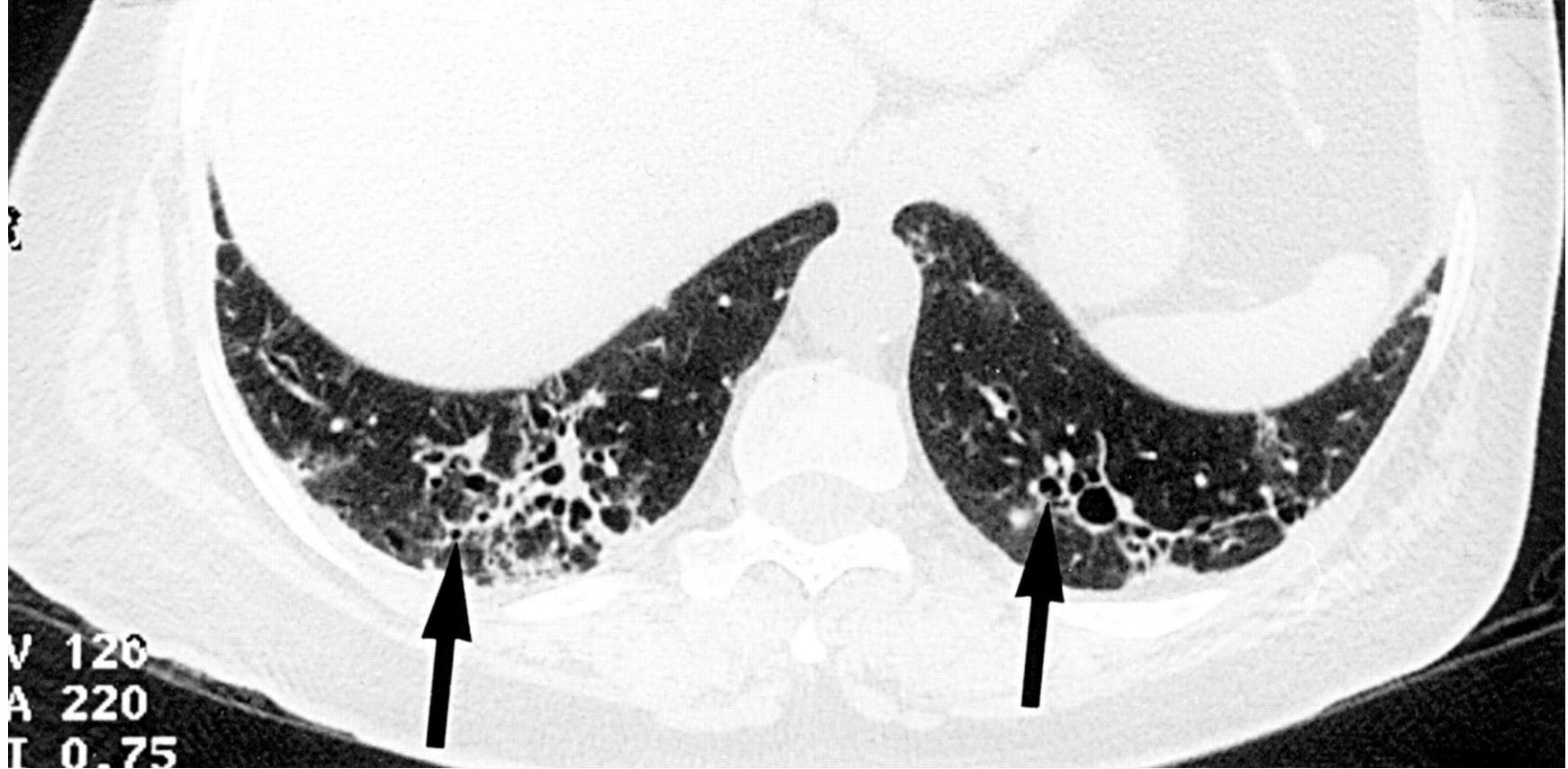
- ▶ Acute Interstitial Pneumonitis – Rare, Acute. As an immunological injury to the lung, medication-related pulmonary toxicity, opportunistic infections.
- ▶ Fibrobullous disease – Similar to that seen in Ankylosing spondylitis.

- ▶ Important to establish underlying histology, response to treatment and prognosis differs.
 - ▶ BOOP/ LIP/ UIP
 - ▶ BAL does not differentiate
 - ▶ Increased lymphocytes, compared to the percentage of Neutrophils and eosinophils, potential for therapeutic responsiveness.
 - ▶ LIP>BOOP>UIP
- 

- ▶ Thoracoscopic open lung biopsy – If imaging and BAL not definitive.
 - ▶ Treatment – Corticosteroids, Cytotoxic drugs
 - ▶ Idiopathic BOOP better response, lesser recurrence, lesser chances for progression to honeycomb lung than CVD associated BOOP
 - ▶ Long term prognosis poor.
- 



Chest radiograph of a 60 year old man, with rheumatoid arthritis and progressive dyspnoea, showing signs of fibrosing alveolitis with basal volume loss and reticular opacities, more pronounced on the right

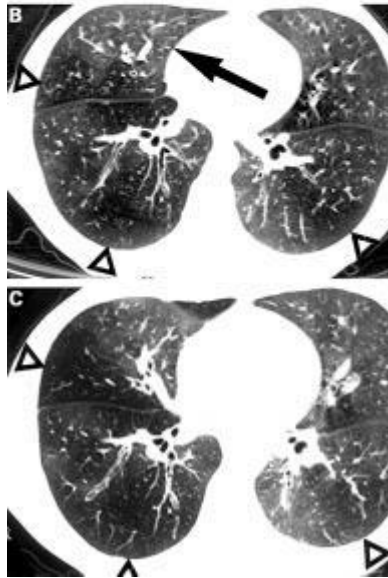


A 66 year old woman with rheumatoid arthritis. HRCT demonstrates peripheral basal fibrosis with architectural distortion and traction bronchiectasis (arrows)



A 37 year old markedly dyspnoeic man with rheumatoid arthritis.

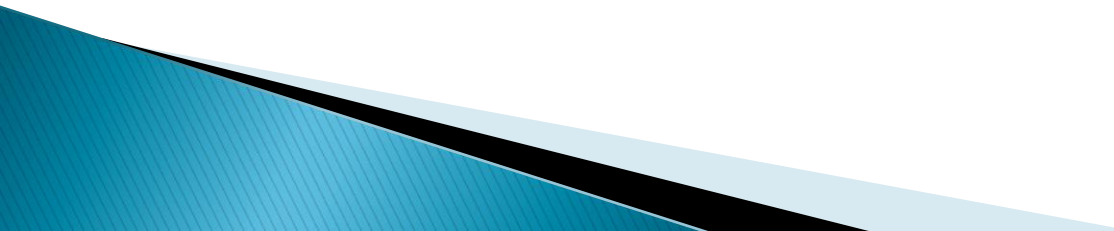
(A) Chest radiograph demonstrates reduced vascularity in the right upper zone and bronchial wall thickening in the lower lobes. The suspected diagnosis was obliterative bronchiolitis.




(B) HRCT in inspiration demonstrates a mosaic attenuation pattern with normal parenchyma (arrow) and extensive areas of reduced vascularity (arrowheads), highly suggestive of obliterative bronchiolitis.

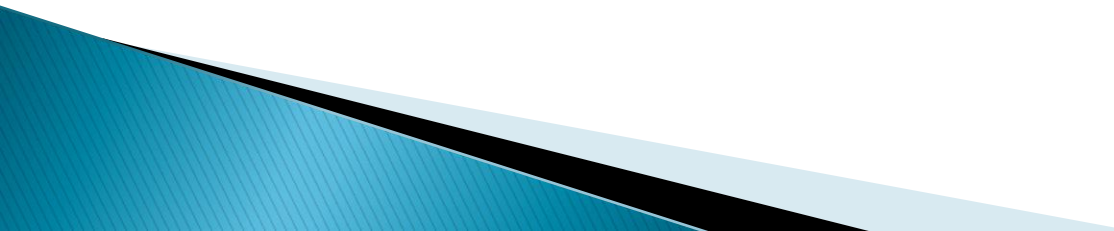
(C) HRCT in expiration confirms the diagnosis by demonstrating air trapping in the areas of reduced vascularity (arrowheads).

Gold induced pneumonitis

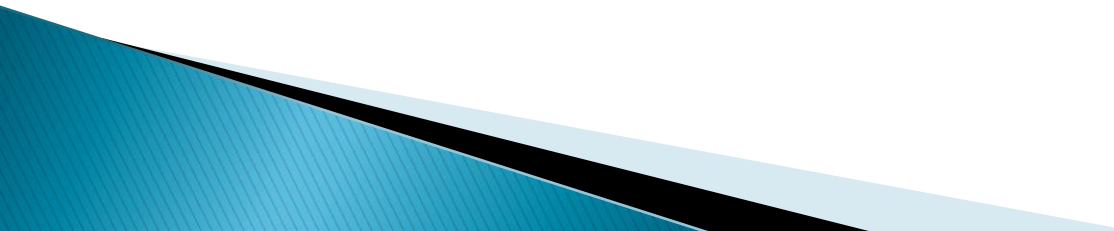
- ▶ Histology – NSIP and BOOP
 - ▶ Dyspnea and cough 4–6 weeks following start of therapy
 - ▶ CXR – Upper mixed alveolar interstitial infiltration
 - ▶ Differentiate from Rheumatoid ILD, withdrawal of the drug results in remission.
- 

Methotrexate pneumonitis

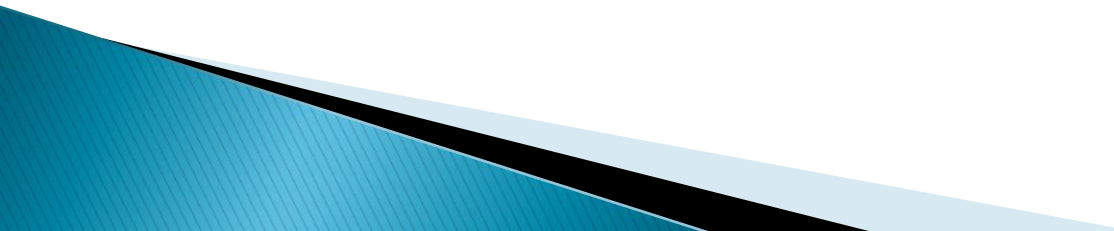
- ▶ Weekly doses 10–20mg
 - ▶ No correlation with Age, sex, duration of disease, or weekly or cumulative dose of the drug.
 - ▶ Incidence – 1–11%
 - ▶ Acute onset cough, fever, Dyspnea, new mixed alveolar and interstitial infiltrates
 - ▶ BAL to differentiate from infectious cause
 - ▶ NSIP/BOOP/Granuloma
 - ▶ Discontinue the drug, i/v Corticosteroids effective.
- 

- ▶ TNF-alpha antagonists have revolutionized therapy for RA patients.
 - ▶ Efficacy in treating Pleuropulmonary complications unknown.
 - ▶ Treatment a/w increased r/o infections, both typical and atypical mycobacteria, fungi, common bacterial pathogens.
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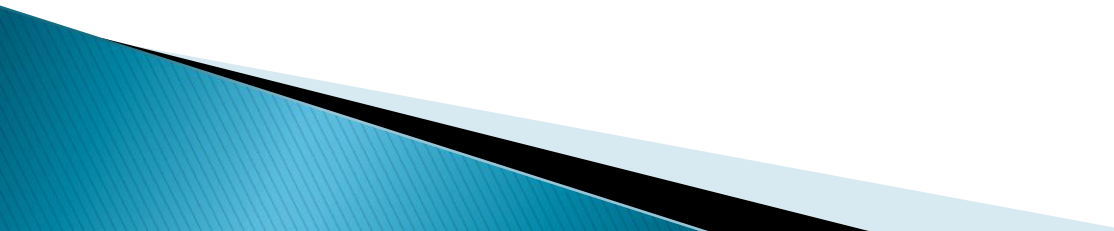
POLYMYOSITIS/DERMATOMYOSITIS

- ▶ Systemic Autoimmune disorder, an inflammatory myopathy.
 - ▶ Dermatomyositis – prominent skin involvement, heliotropic rash, Gottron's papules/rash, less severe myositis.
 - ▶ Pulmonary complications are common 40%
 - ▶ Often predate or overshadow the muscle or skin manifestations.
- 

Manifestations

- ▶ Aspiration Pneumonia
 - ▶ Respiratory muscle dysfunction
 - ▶ Interstitial lung Disease
 - ▶ Unlike other CVDs, Airways and pleura are not involved primarily
 - ▶ Pulmonary hypertension (plexogenic arteriopathy) in cases in which crossover with Scleroderma is suspected.
- 

Aspiration Pneumonia

- ▶ Common 10–20%
 - ▶ Dysphagia in 50%
 - ▶ Striated muscles of the hypopharynx and upper esophagus.
 - ▶ Loss of normal swallowing, failure to protect the airway.
 - ▶ More likely in patients with extensive skin or muscle involvement.
- 



ASPIRATION PNEUMONIA

Respiratory Muscle dysfunction

- ▶ Uncommon <5%
- ▶ Extensive myositis involving the respiratory muscles and diaphragm, Hypercapnic respiratory failure.
- ▶ Less extensive involvement, reduction in cough generation, hypostatic pneumonia, atelectasis d/t mucus plugging.
- ▶ CXR – Elevated hemidiaphragms and basal atelectasis
- ▶ Weakness causes a restricted physiological defect, tachypnea and dyspnea in the face of normal DLCO, normoxemia, and hyperventilation.


MALIGNANCY

There is a higher than expected incidence of neoplastic disease, particularly lung carcinoma, with a higher rate mortality from cancer in patients with dermatomyositis.

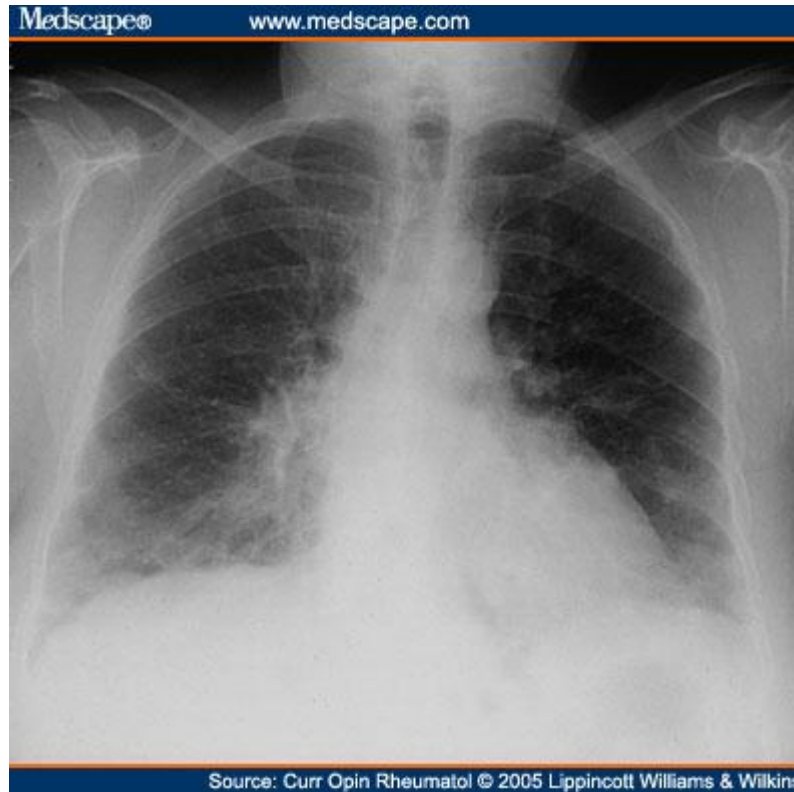
Symptoms of PM/DM may predate the tumour by one to two years.



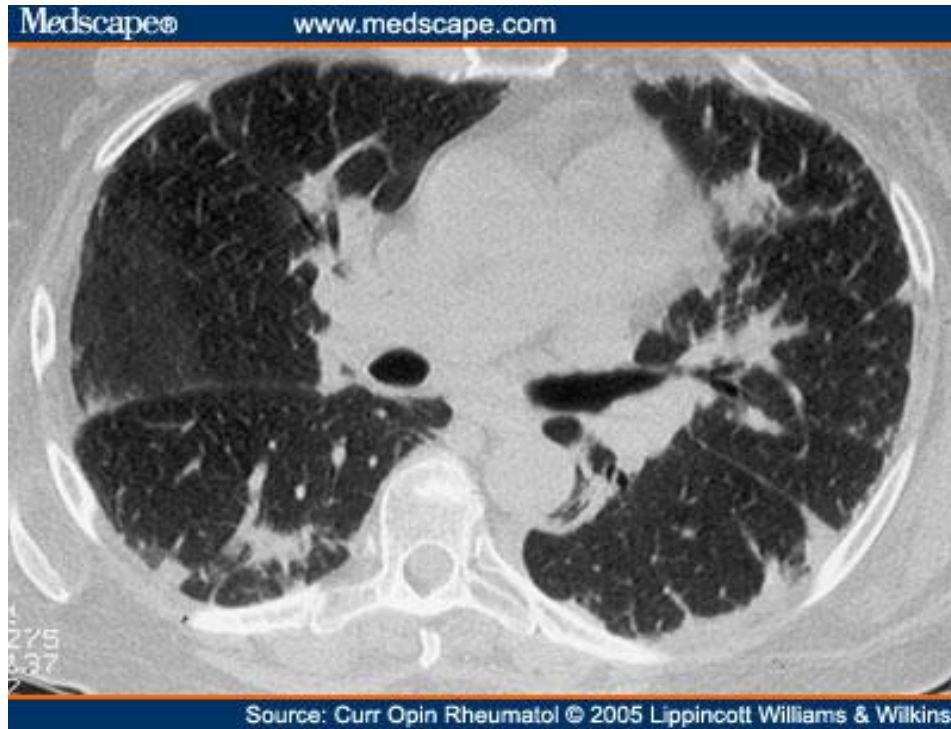
Interstitial Lung Disease

- ▶ Prevalence 5–30%
 - ▶ Significantly higher incidence in Japan 40–80%
 - ▶ Histological type NSIP (based on the revised classification system)
 - ▶ Others – DAD, BOOP, DAH
 - ▶ No relationship with the extent of muscle or skin disease, level of CPK elevation, presence of serum RA factor or ANAs.
 - ▶ Relationship with anti-Jo-1 antibody.
- 

- ▶ All ILDs in PM/DM more common in women
- ▶ Chronic cough, progressive dyspnea
- ▶ Clubbing rare
- ▶ CXR – Reticulonodular infiltrates, with disease progression reduction of lung volume, honeycomb lung, pulmonary hypertension.
- ▶ Overall, peripheral air space consolidation and peribronchial thickening are fairly characteristic of pulmonary involvement in PM/DM and there is a relatively lower incidence of honeycombing.
- ▶ PFTs – Restrictive pattern, low DLCO
- ▶ Treatment – More cellular disease, more responsive
- ▶ Corticosteroids
- ▶ Resistant cases – Cyclophosphamide, cyclosporine, tacrolimus



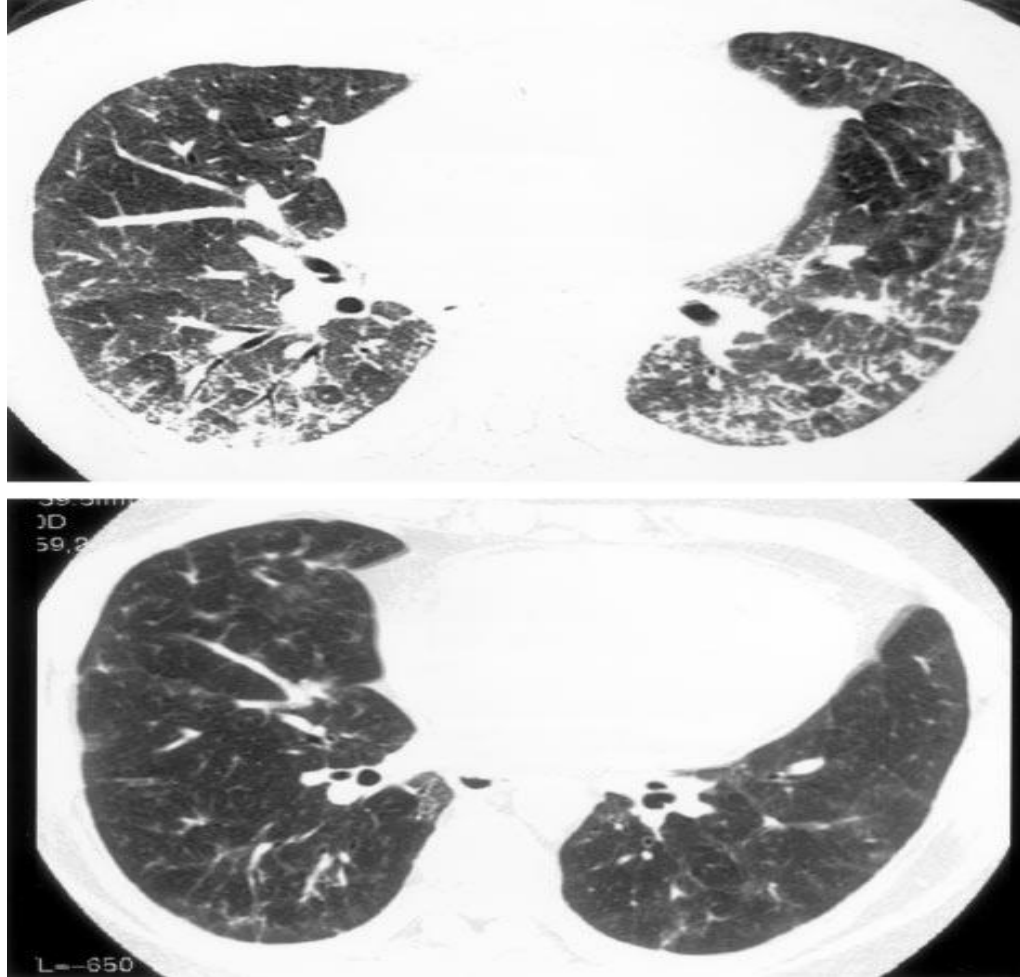
Chest radiograph. Chest radiograph of a 65-year-old woman with recent onset of polymyositis demonstrates bilateral diffuse opacities subpleural, particularly at the lung bases



High-resolution computerized tomography of lungs. High-resolution computerized tomography of lungs of a 65-year-old woman with recent onset of polymyositis showing consolidation, subpleural opacities and thickening of interlobular pleura and bronchial wall

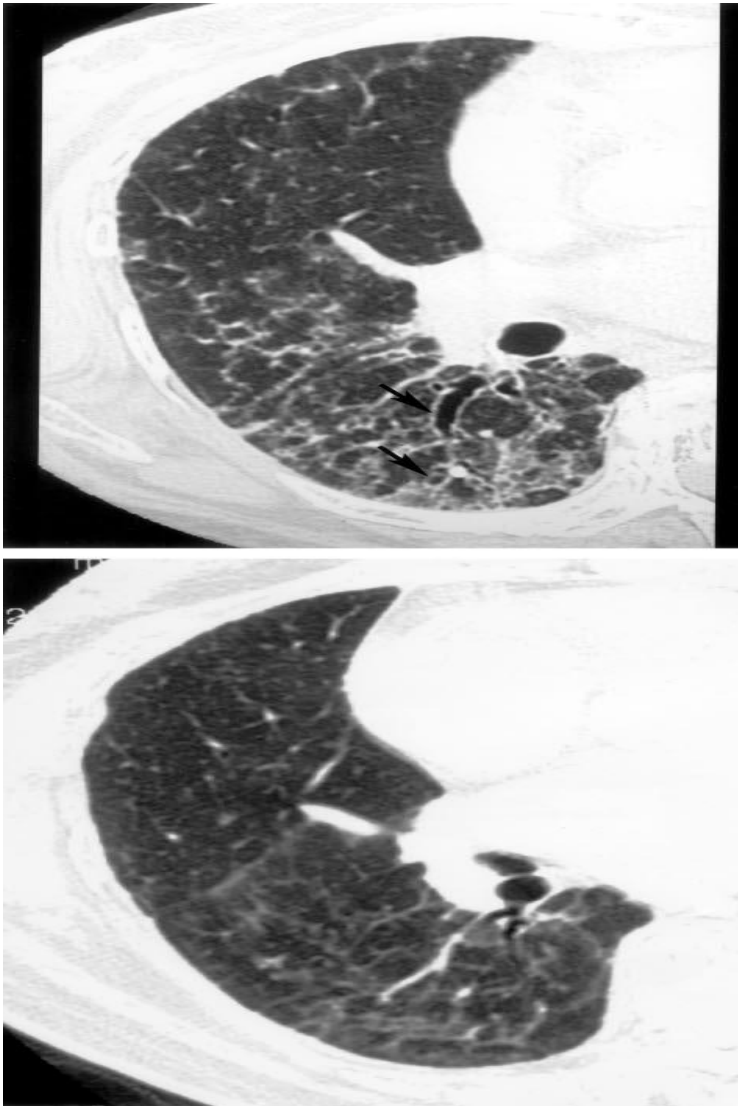


Chest X-Ray AP supine showing a right basal subpleural triangular focus of consolidation as well as prominent interstitial markings.



A 57-year-old man with NSIP and PM

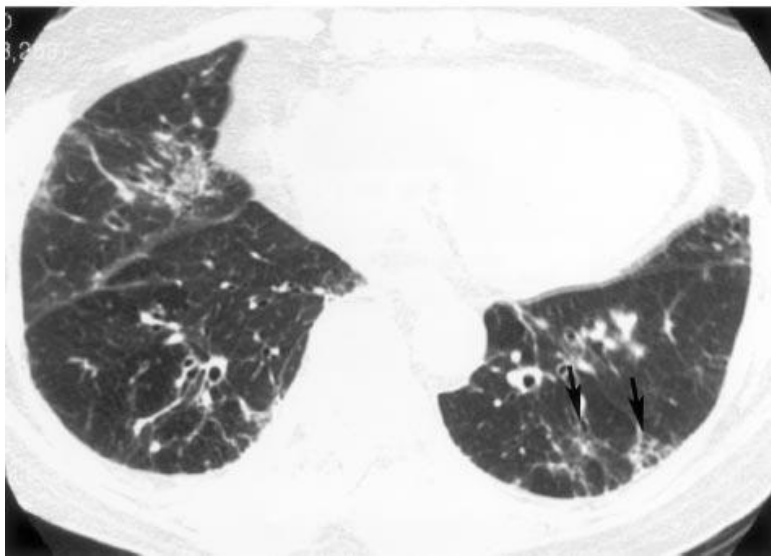
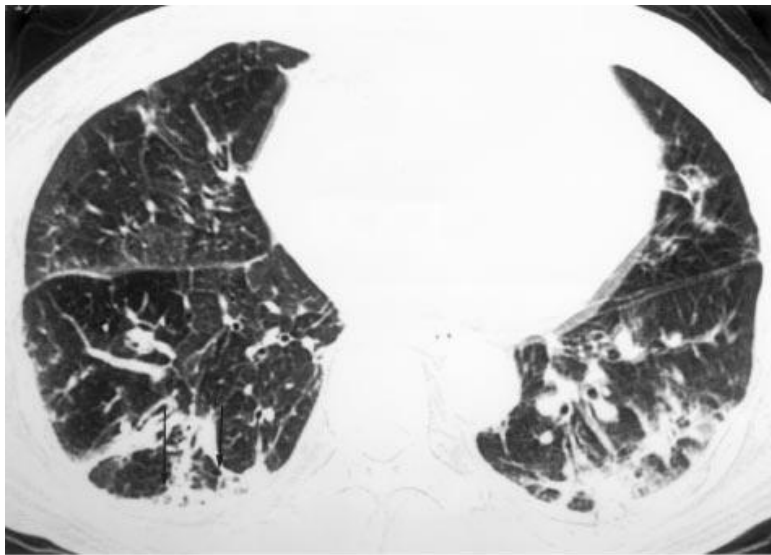
Top: the initial high-resolution CT scan shows diffuse bilateral ground-glass and reticular opacities. The abnormalities involve both central and peripheral lung zones. Bottom: a follow-up high-resolution CT scan obtained 22 months later shows significant improvement of the ground-glass and reticular opacities.



A 66-year-old woman with NSIP and DM.

Top: the initial high-resolution CT scan shows diffuse reticular and ground-glass opacities, as well as traction bronchiectasis (arrows).

Bottom: follow-up high-resolution CT scan obtained 33 months later shows improvement of the reticular and groundglass opacities. Traction bronchiectasis also showed significant improvement in this patient.



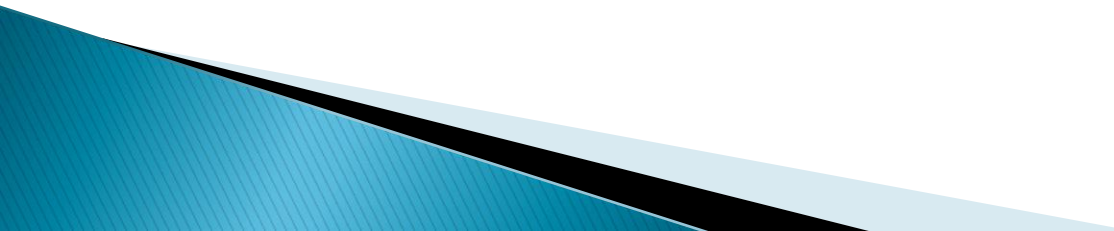
A 63-year-old woman with NSIP and DM.

Top: high-resolution CT scan of the lung bases showing a thickening of the septal lines and peripheral consolidation. Septal line thickening involves both the central and peripheral areas.

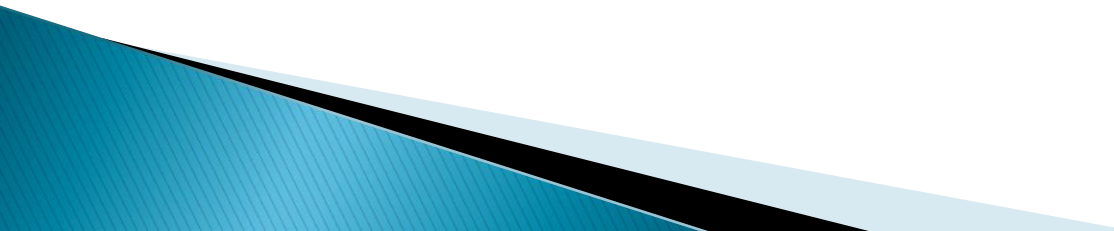
Note that dilated bronchi are located at the lung periphery inside and adjacent to areas of consolidation (arrows).

Bottom: a follow-up high-resolution CT scan obtained 14 months later.

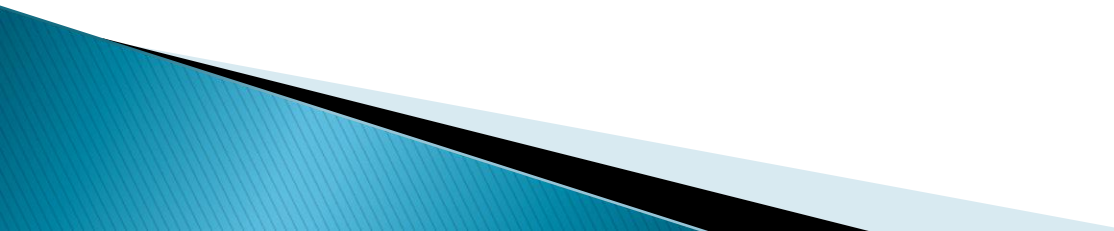
There is a disappearance of consolidation and an improvement of reticular opacity. Ground-glass opacity developed in the areas of previous consolidation (arrows).

- ▶ In PM/DM, an **Acute pulmonary presentation**, clinical and radiographic picture reminiscent of diffuse infectious pneumonia.
 - ▶ Underlying lesion **DAD**
 - ▶ Severe respiratory failure
 - ▶ Recovery unusual despite aggressive anti-inflammatory, immunosuppressive therapy.
 - ▶ **BOOP** – acute/subacute
 - ▶ **Differentiation from DAD** – important because marked disparity in treatment outcome and survival.
 - ▶ In BOOP, corticosteroid responsiveness with or without an additional agent is the rule rather than the exception.
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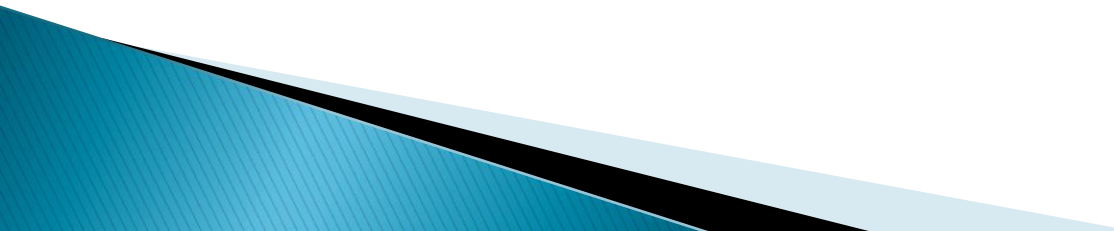
MIXED CONNECTIVE TISSUE DISORDER

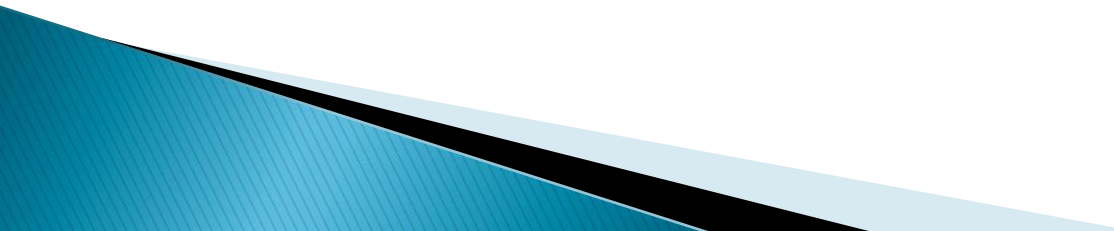
- ▶ MCTD
 - ▶ F/o SLE, PM/DM, and scleroderma
 - ▶ Characterised by Anti-RNP
 - ▶ Affecting women in their 30s to 50s.
 - ▶ Pleuropulmonary complications frequent 20–80%
 - ▶ Pleural disease, Pulmonary vascular disease, Aspiration Pneumonia, Respiratory Muscle dysfunction, Interstitial Lung Disease.
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Pleural Disease

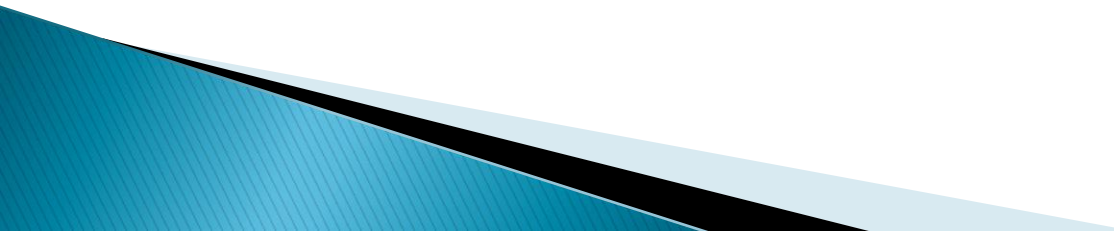
- ▶ Pleurisy in 40%
 - ▶ Pleural effusions uncommon 5%
 - ▶ Exudative effusion
 - ▶ Very little information concerning its characteristics is available in literature.
- 

Pulmonary Vascular disease

- ▶ *Pulmonary hypertension* – by recurrent pulmonary emboli, hypoxic vasoconstriction secondary to ILD, or plexogenic arteriopathy.
 - ▶ Incidence unknown but very common.
 - ▶ Women
 - ▶ Dyspnea and fatigue
 - ▶ Normal CXR except pulmonary arterial enlargement, and an isolated reduction in the DLCO
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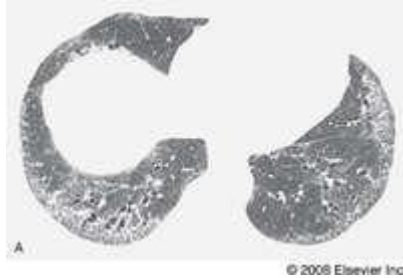
- ▶ Medium-size pulmonary artery *vasculitis*
 - ▶ Immunologic mediated injury with deposition in the walls (IgG, C3)
 - ▶ Circulating Lupus anticoagulant (Anti phospholipid syndrome) may complicate the course, predisposing them to thromboembolic disease.
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Aspiration Pneumonia

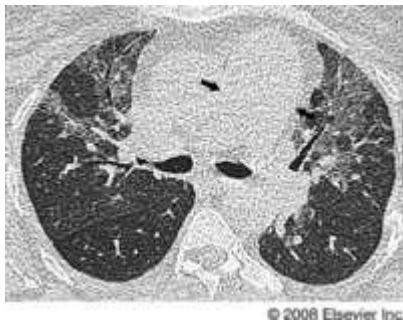
- ▶ Common
 - ▶ In those with predominant features of Scleroderma, or PM/DM
 - ▶ Esophageal dysmotility and dilatation reflux esophagitis, recurrent aspiration pneumonia
 - ▶ Incidence of abnormal esophageal manometry > 50%, around 74%
- 

Interstitial Lung Disease

- ▶ Commonest
- ▶ Increased incidence compared to other CVDs
- ▶ 80%(using physiological criteria)
- ▶ Thirty per cent of patients have signs of interstitial lung disease on chest radiography at presentation.
- ▶ Histology – NSIP and/or UIP
- ▶ Progress to honeycomb lung esp in those with f/o Scleroderma
- ▶ Same C/F
- ▶ DAH – few cases, similar in presentation to that in SLE
- ▶ Mediastinal LAP



Nonspecific interstitial pneumonia in mixed connective tissue disease (MCTD). High-resolution CT shows bilateral ground-glass opacities, fine reticulation, traction bronchiectasis, and traction bronchiolectasis mainly in the peripheral lung regions. Note the relative sparing of the subpleural lung in the dorsal regions, a feature characteristic of NSIP. The patient was a 43-year-old woman with MCTD and NSIP-pattern on CT



Pulmonary hypertension and fibrotic lung disease in mixed connective tissue disease. High-resolution CT shows bilateral ground-glass opacities and mild reticulation and traction bronchiectasis in a bronchovascular distribution. Also note dilatation of the pulmonary artery (*arrowheads*).




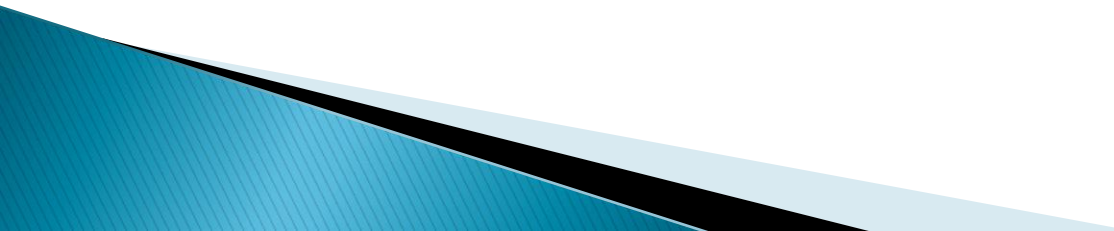
Pulmonary hypertension in mixed connective tissue disease. Contrast-enhanced CT shows marked dilatation of the main, right and left pulmonary arteries. Also note enlarged bronchial arteries (*arrow*). The patient was a 44-year-old woman with mixed connective tissue disease and severe pulmonary artery hypertension




Honeycombing in mixed connective tissue disease (MCTD). High-resolution CT shows marked honeycombing and a dilated esophagus. The patient was a 55-year-old woman with MCTD. The histologic sub-type of the fibrosis was not established, the pattern is suggestive of usual interstitial pneumonia.

ANKYLOSING SPONDYLITIS

- ▶ Seronegative spondyloarthropathy
 - ▶ Pulmonary involvement 1.3–15%
 - ▶ Ankylosis of costovertebral joints.*
 - ▶ Reduced chest wall mobility.*
 - ▶ May eventually result in fixation of the chest wall
 - ▶ Mild to moderate restrictive lung disease
 - ▶ No Muscular involvement, Diaphragmatic function is preserved
 - ▶ No Ventilatory failure.
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- ▶ Incidence of ILD complication <2%
 - ▶ Histology – UIP
 - ▶ Predilection for the Upper lung Zones (contrast with other CVDs)
 - ▶ Only appears late in the course of AS, never precedes it (contrast with other CVDs).
 - ▶ Treatment with corticosteroids is ineffective, therefore not indicated
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- ▶ APICAL FIBROBULLOUS DISEASE
 - ▶ CXR – Fibrocystic Disease, honeycombing
 - ▶ HRCT—This demonstrates abnormalities in 69%–71%, including interlobular septal thickening, basal interstitial lung disease, bronchiectasis (primary and traction), emphysema, upper lobe fibrosis, pleural thickening, mycetoma formation, and mediastinal lymphadenopathy.
 - ▶ Tracheobronchomegaly (Mounier–Kuhn syndrome) has been reported
 - ▶ Most serious complication – infection with invasive aspergilla spp., atypical mycobacteria, saprophytic colonization of the cysts by aspergilla (Aspergilloma), life threatening hemoptysis.
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Ankylosing spondylitis– bell shaped chest, fusion of costotransverse and costovertebral joints. Parallel linear densities in the upper mediastinum represent thoracic syndesmophytes.



Occurs late in the course of disease, restrictive pulmonary function with a high residual functional capacity and vital capacity unlike progressive idiopathic scoliosis. "Fibrobullous" upper lobe disease is rarer occurring in approx 1% of cases after a 15–20year period.



05/26/72

Upper lobe disease
Ankylosing spondylitis



**Thanks for your
attention!**