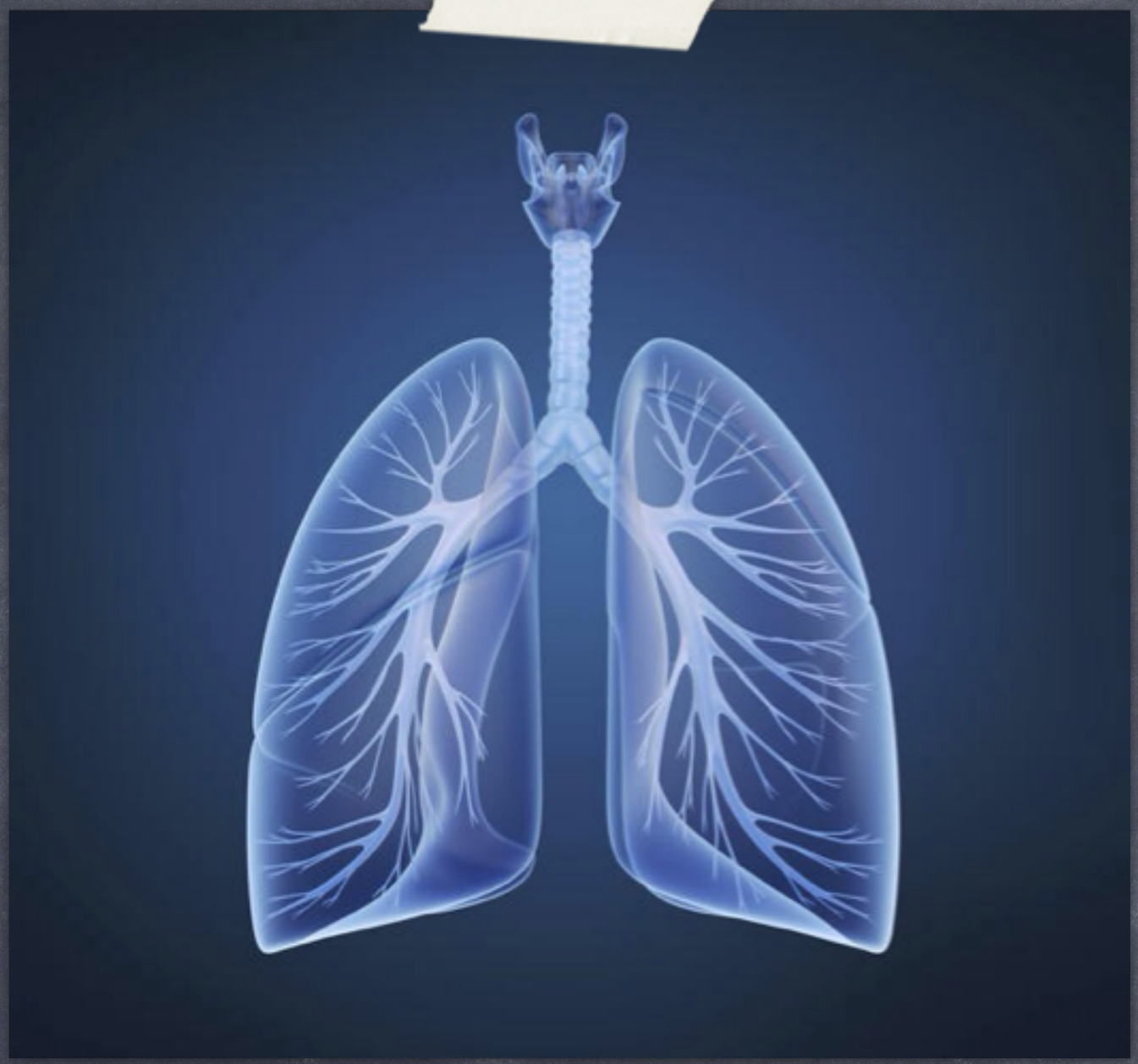
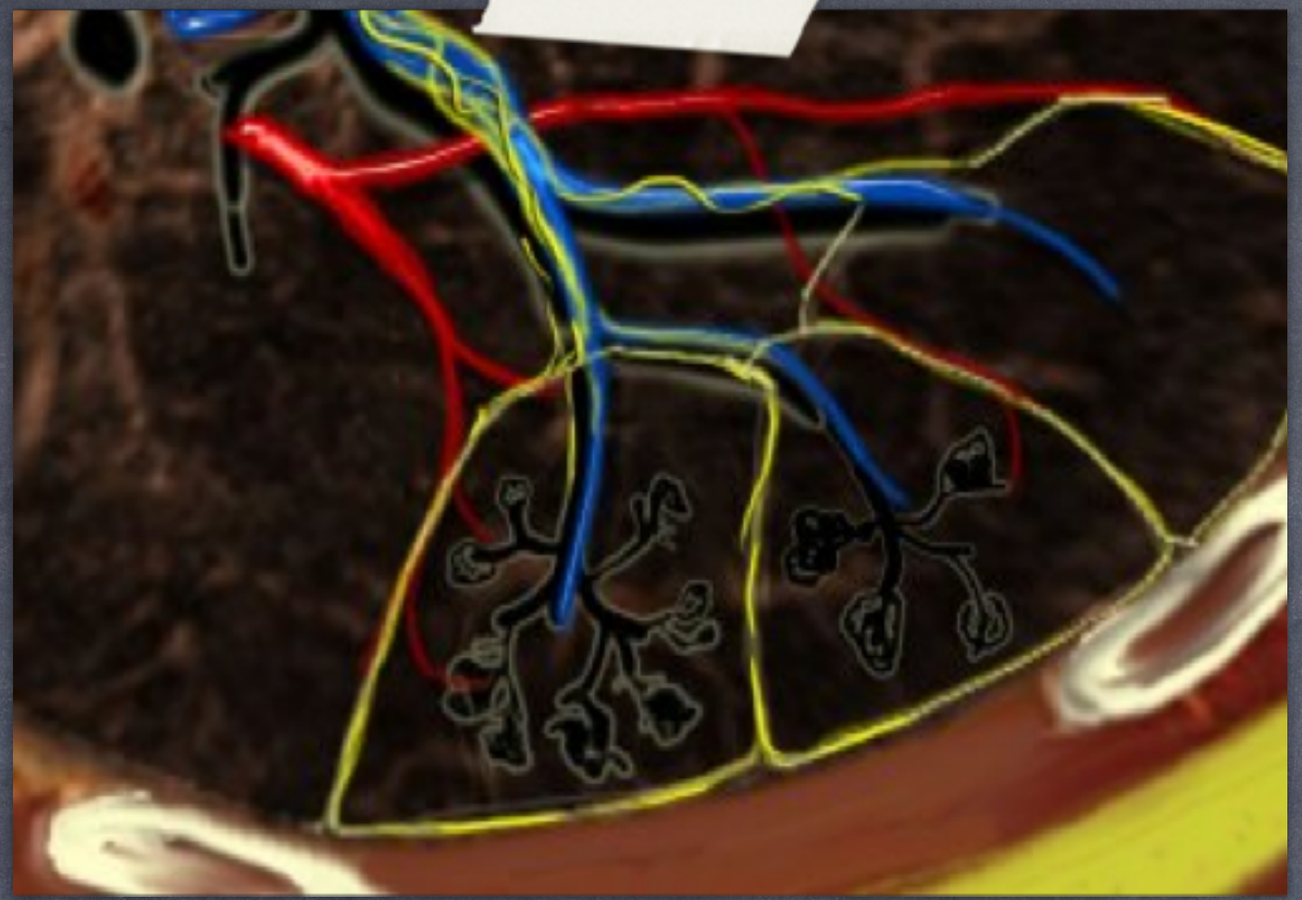


Practical approach to interstitial lung diseases

Hamdi Turkey - Pulmonologist



The interstitium of the lung is not normally visible radiographically; it becomes visible only when disease (e.g., edema, fibrosis, tumor) increases its volume and attenuation.

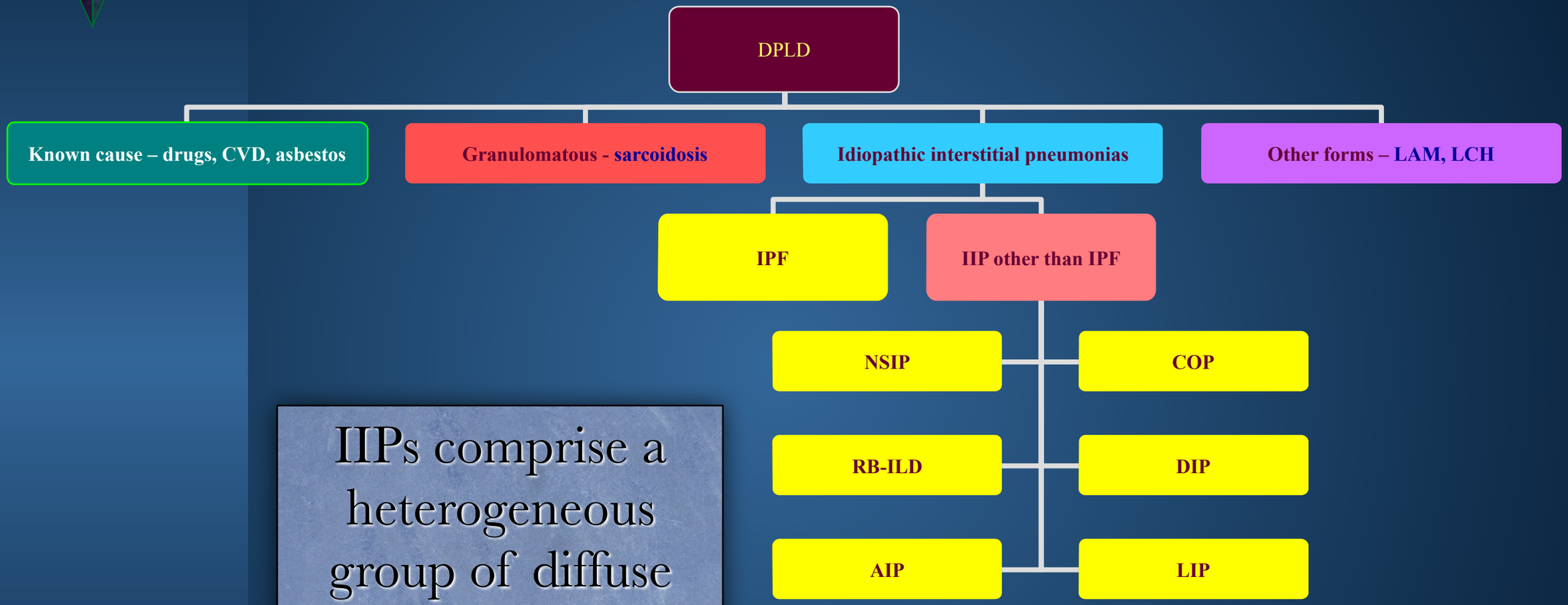
The interstitial space is defined as continuum of loose connective tissue throughout the lung composed of three subdivisions:

(i)the bronchovascular (axial), surrounding the bronchi, arteries, and veins from the lung root to the level of the respiratory bronchiole

(ii) the parenchymal (acinar), situated between the alveolar and capillary basement membranes

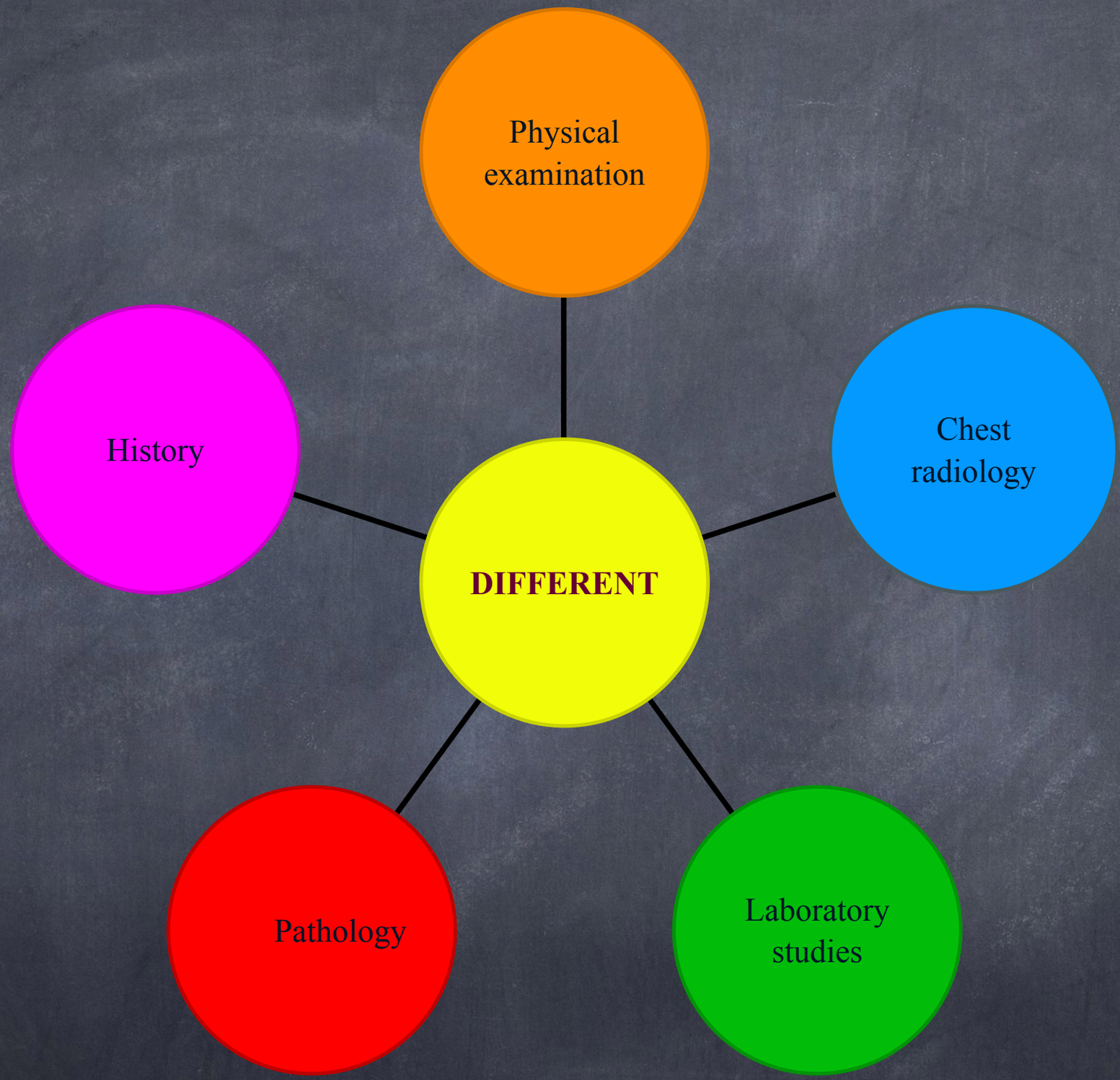
(iii) the subpleural, situated beneath the pleura, as well as in the interlobular septae.

Idiopathic Interstitial Pneumonias



IIPs comprise a heterogeneous group of diffuse parenchymal lung diseases (DPLD) of unknown cause

Include seven entities


Physical examination
History
Chest radiology
DIFFERENT
Pathology
Laboratory studies

Classification - Idiopathic Interstitial Pneumonias
(ATS/ERS joint consensus statement - 2002)

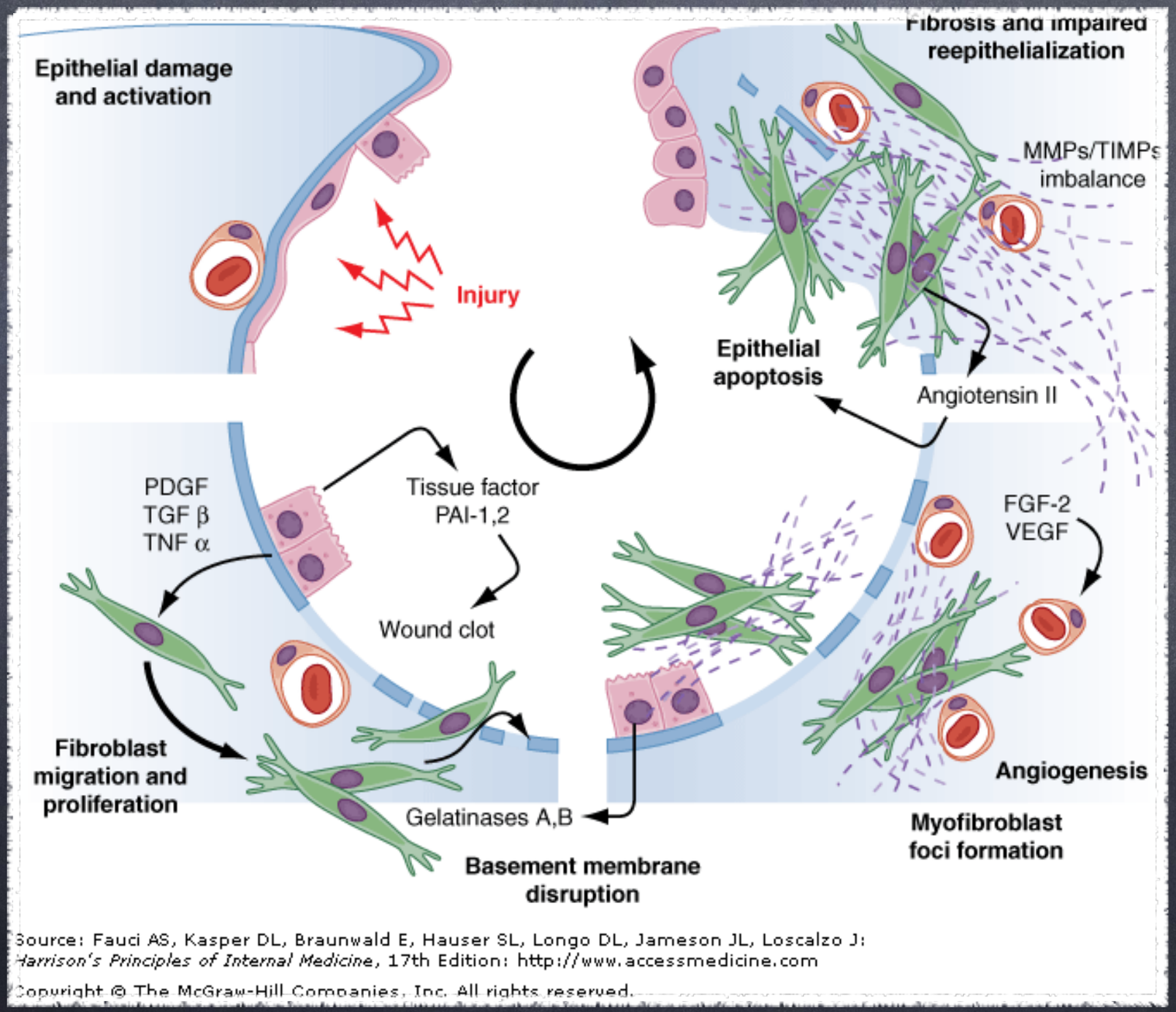
- **Based mainly on histological patterns / in order of relative frequency**

1. **Idiopathic pulmonary fibrosis (IPF) / Usual interstitial pneumonia (UIP)**
2. **Non-specific interstitial pneumonia (NSIP)**
3. **Cryptogenic organizing pneumonia (COP) / Bronchiolitis obliterans organizing pneumonia (BOOP)**
4. **Acute interstitial pneumonia (AIP) / Diffuse alveolar damage (DAD)**

- **Respiratory bronchiolitis-associated interstitial lung disease (RB-ILD)**
- **Desquamative interstitial pneumonia (DIP)**

1. **Lymphoid interstitial pneumonia (LIP)**

IIPs represent fundamental responses of the lung to injury



Source: Fauci AS, Kasper DL, Braunwald E, Hauser SL, Longo DL, Jameson JL, Loscalzo J: *Harrison's Principles of Internal Medicine*, 17th Edition: http://www.accessmedicine.com

Idiopathic Interstitial Pneumonias

- **Do not represent 'diseases' per se**
- **Idiopathic - unknown cause**
- **Interstitial pneumonia - injury to lung parenchyma by varying patterns of inflammation and fibrosis**
- **All truly idiopathic or cryptogenic?**
  - **Common findings in collagen vascular diseases and drug-related lung diseases**

Idiopathic Interstitial Pneumonias Diagnosis

- **Achieving the correct diagnosis is a dynamic process**
  - **diagnosis may take time**
  - **may have to be revised at several stages**

- **Final diagnosis only after all the data have been reviewed by**
  - **Pulmonologist**
  - **Radiologist**
  - **Pathologist**

- **Clinico-radiologic-pathologic diagnosis**
  - **C-R-P diagnosis**

History

- **Nature of the first symptoms**
  - **dyspnoea /OE, cough +/–, little sputum**
- **Progression**
- **Comorbid diseases**
  - **CTD – arthritis, rashes, raynaud's, dysphagia**
  - **Immune deficiency diseases**
  - **Drugs**
- **Environmental / occupational exposures - with dates & durations**
  - **Asbestos, silica**
- **Smoking status**
- **Previous malignancies and treatment**
- **Family history of lung diseases**

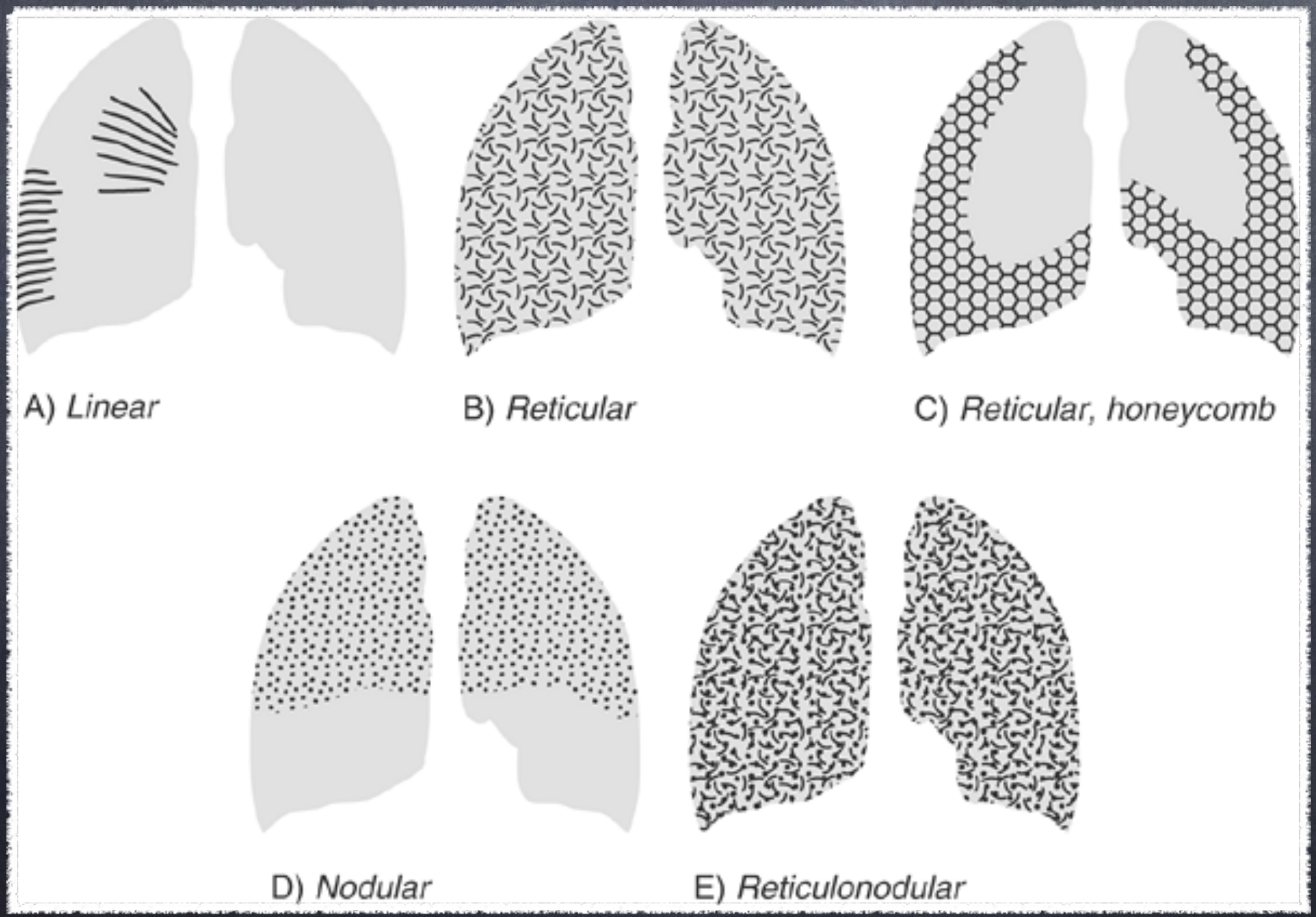
Examination

- **Breathless**
- **Plethoric**
- **Finger clubbing**
- **Skin – rashes, ulcers, tethering**
- **Joint swelling**
- **Leg oedema**
- **P_2**
- **Lung crackles**
  - **end-inspiratory**
  - **Fine dry or “Velcro”-type**

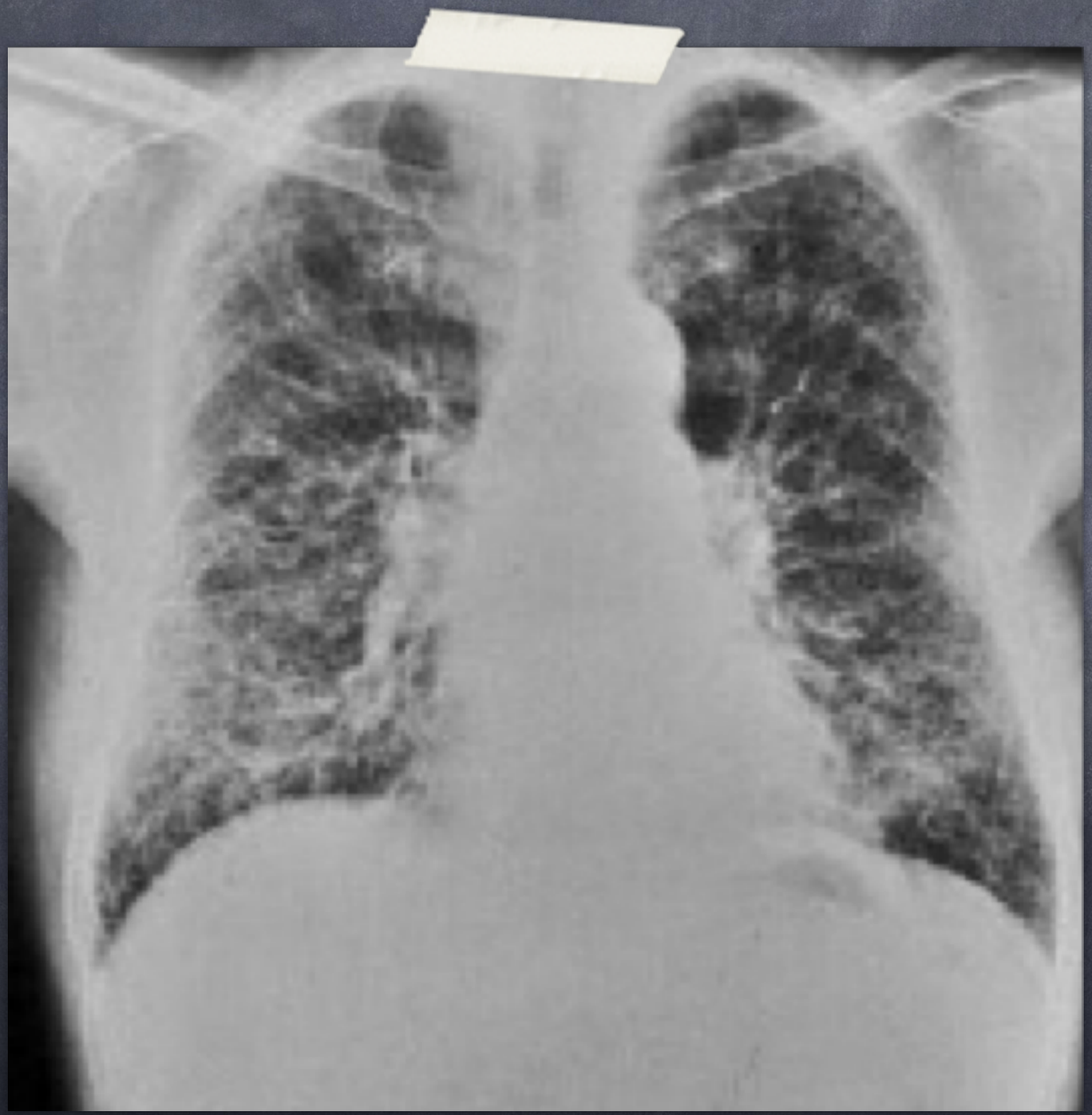
Radiology

- **Interstitial lung disease may result in four patterns of abnormal opacity on chest radiographs and CT scans: linear, reticular, nodular, and reticulonodular**
- **These patterns are more accurately and specifically defined on CT**

Radiological patterns

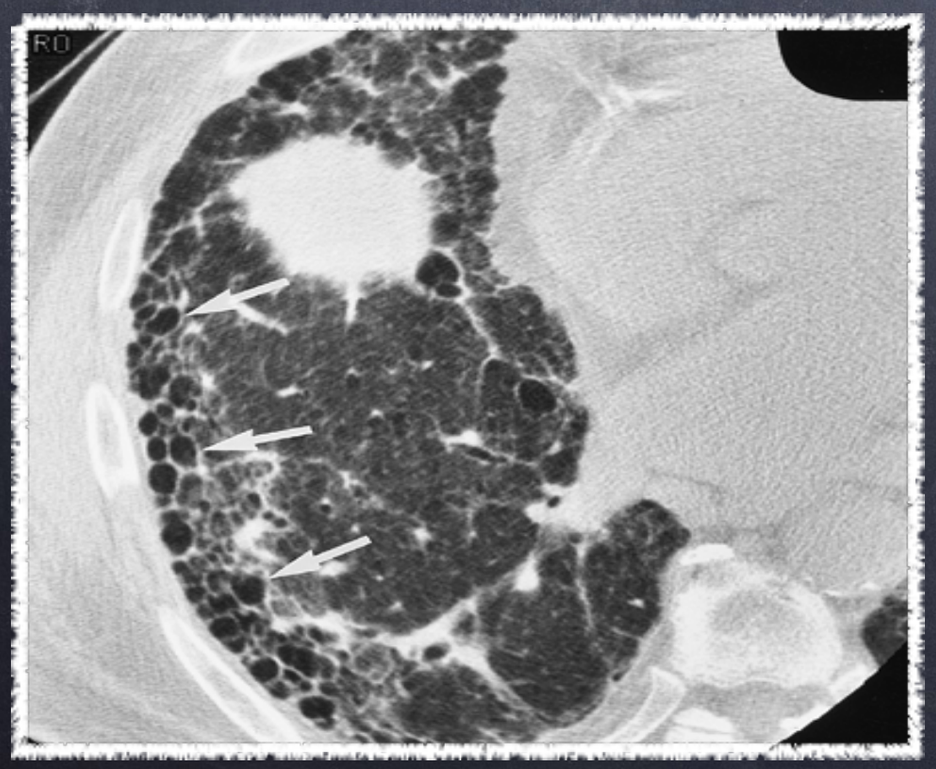


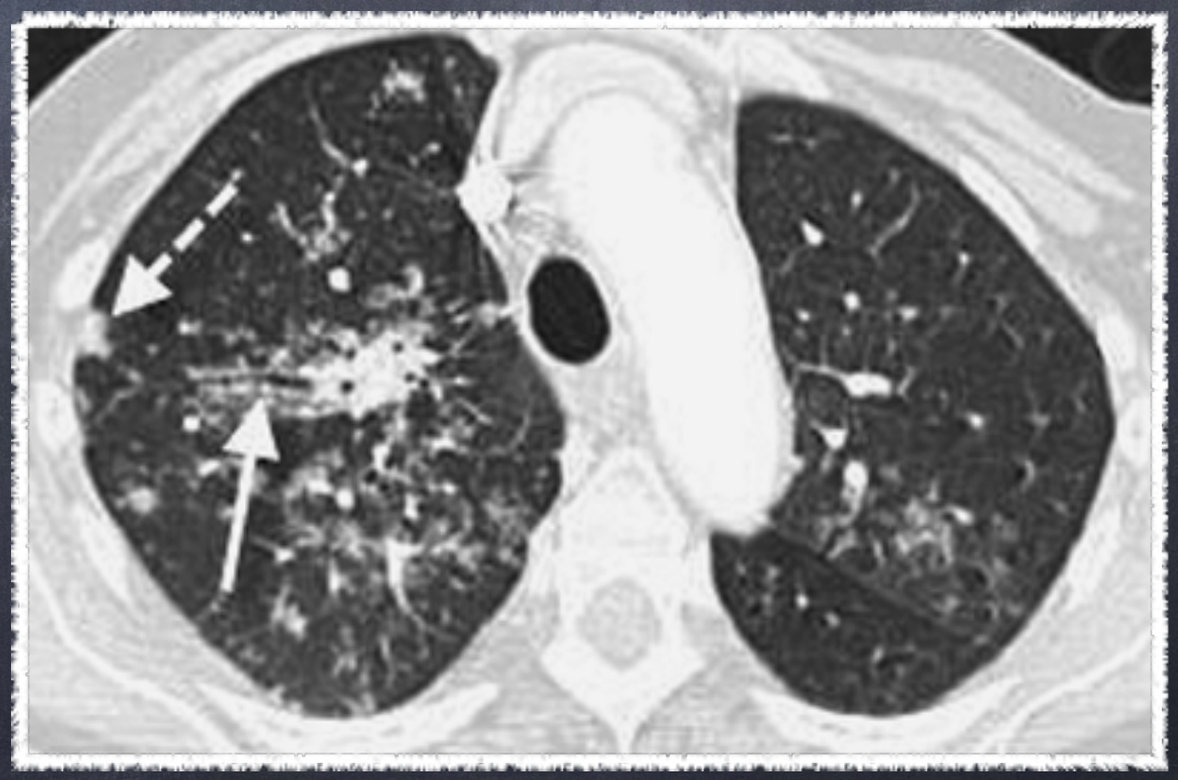
CXR



HRCT

- For almost all pts with possible IIP
- Require
  - Correct radiological technique
  - Experienced radiologist





What is next?

HRCT

- Confident- UIP
- Confident- UIP
- Confident- UIP
- Confident- UIP

Biopsy

Surgical lung biopsy

- Waiting for clinical / radiological deterioration before obtaining biopsy is not recommended
  - Delays diagnosis
  - Least helpful when obtained late in the course of the illness or after commencement of treatment
  - Pt receives unnecessary or inappropriate treatments

- CTD-associated ILD – biopsy is not usually performed

Benefits of Surgical lung biopsy

- Establishes a firm clinicopathological diagnosis
- Prevents unnecessary exposure to toxic treatments
- Confirms or excludes alternative diagnoses
  - sarcoidosis, LAM, LCH, PAP, lymphangitis carcinomatosis, occupational diseases

FOB

- TBLB
  - Not useful for most IIPs
    - except AIP and occasionally COP
    - Tissue obtained is very small
    - May not be representative
  - 1^{ry} role is to exclude sarcoidosis, neoplasms and certain infections
- BAL
  - Not essential
  - Done as part of the diagnostic workup of a DPLD
    - to exclude infection, tumour
    - Rarely diagnostic – PAP, LCH

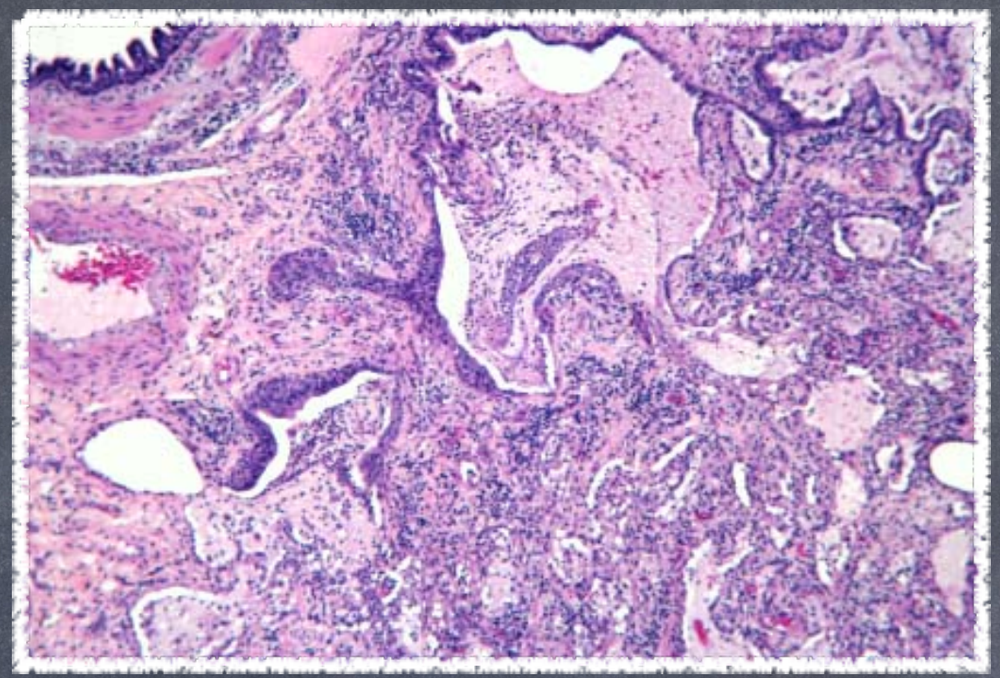
IPF/ UIP

- UIP is a histological diagnosis
- Has distinctive HRCT findings and they are usually shown at lung biopsy
- If the UIP pattern is of unknown cause the disease is called
  - Idiopathic pulmonary fibrosis (IPF)
- IPF accounts for more than 60% of the cases of UIP

IPF/ UIP

- Requires exclusion of other known causes of UIP
  - Drug toxicities – a long list
    - Commonly cytotoxic agents
  - Environmental exposures (asbestos, silica)
  - Collagen vascular diseases

UIP histology criteria



- Key features
1. Dense fibrosis with frequent honeycombing
2. Fibroblastic foci at the edges of the scars
3. Patchy lung involvement
4. Subpleural and paraseptal distribution

- Pertinent negative findings
1. Lack of active lesions of other DPLDs
2. Lack of marked interstitial chronic inflammation
   - Granulomas – inconspicuous or absent
1. Lack of substantial organic dust deposits - asbestos
2. Lack of marked eosinophilia

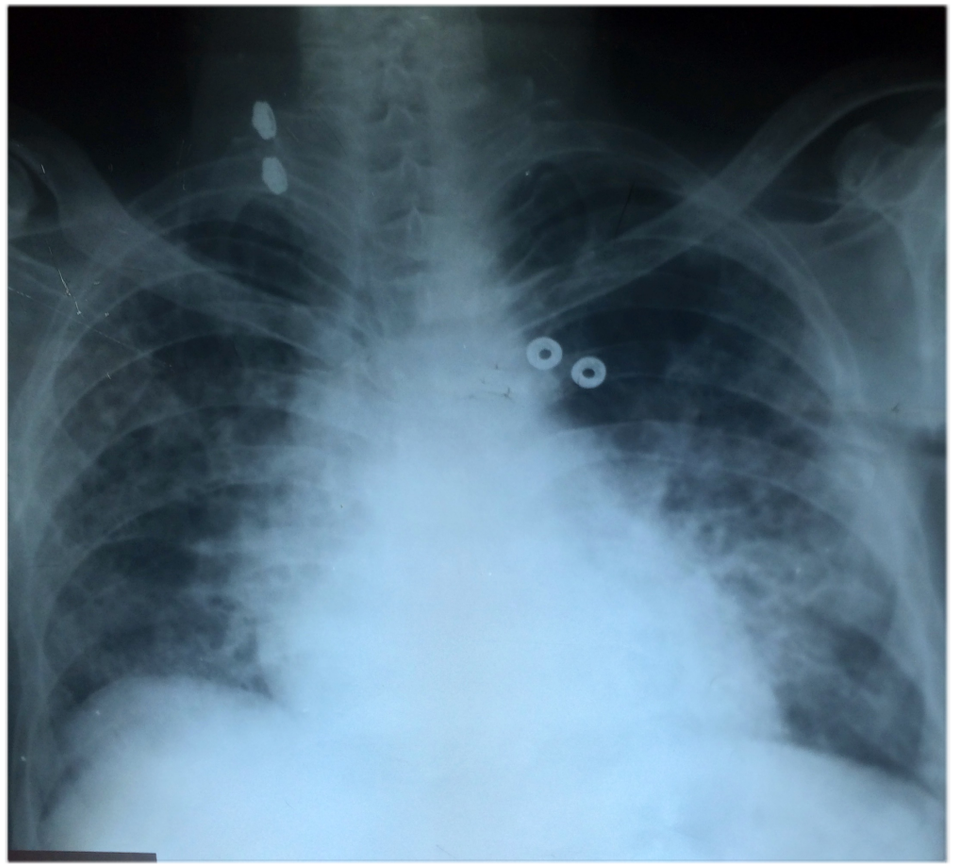
Clinical features

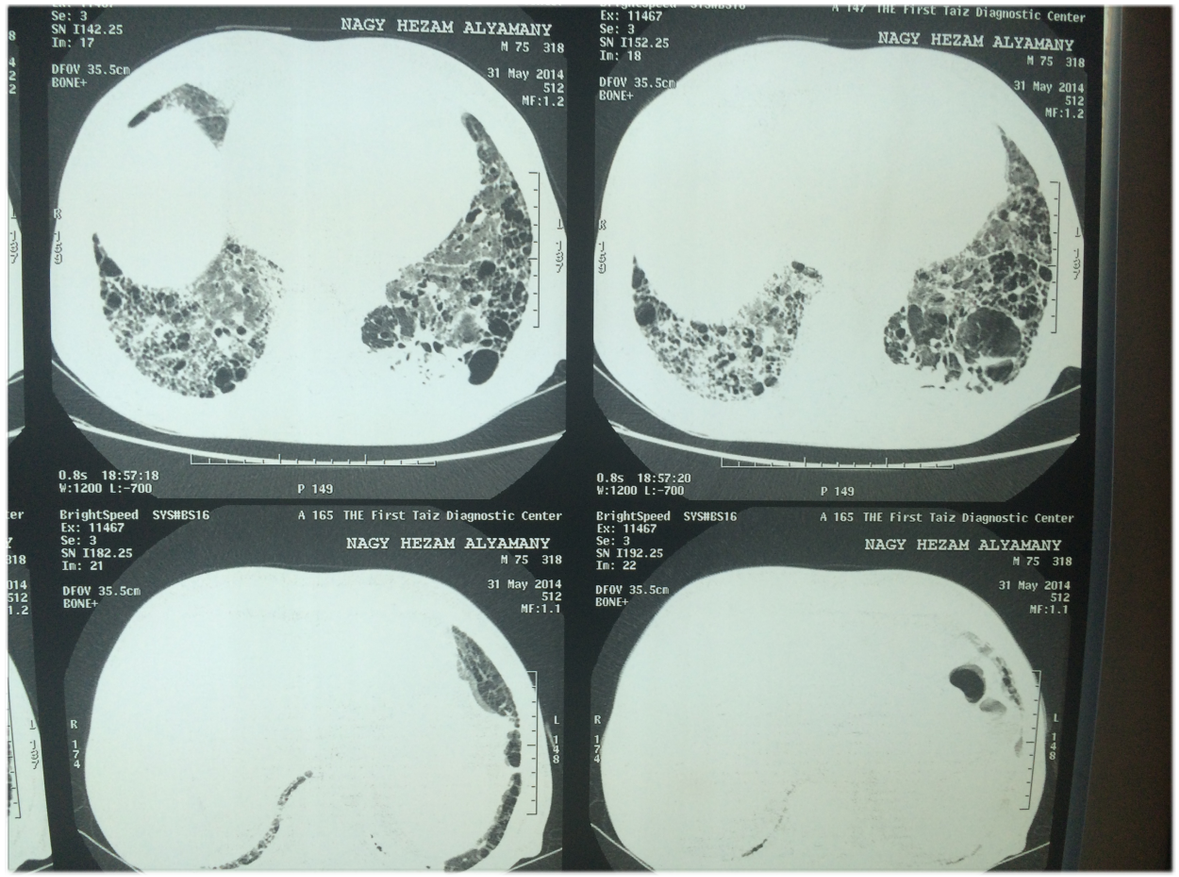
- Age of onset > 50 yrs
  - –usually present > 6/12 after the onset
- M > F – slightly
- Dyspnoea
  - –the most prominent and gradual
  - –Occasionally – periods of rapid decline
    - accelerated phase
      - intercurrent viral infection
    - development of organizing pneumonia
    - Diffuse alveolar damage
- Cough – paroxysmal
- Constitutional symptoms – unusual

Clinical features

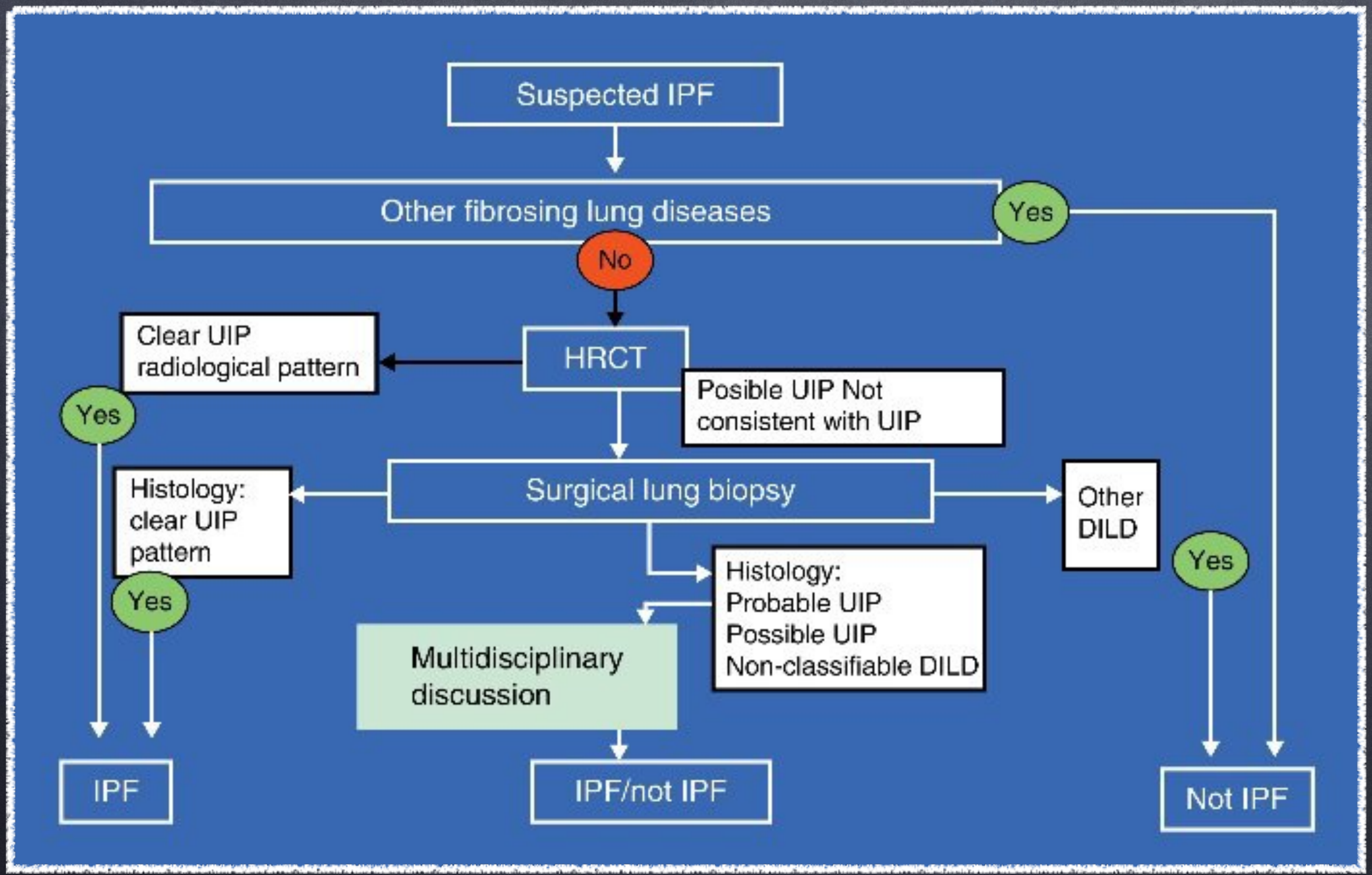
- Finger clubbing – 25-50%
- Fine end-inspiratory crackles
  - bases → other areas
- Rt. Ht failure & leg oedema
- Medium length of survival 2.5-3.5 yrs

- BAL
  - Neutrophil α extent of reticular damage
  - E - mild – moderate
  - L - not a feature





- Peripheral reticular opacities
  - –most marked at the bases
- Honeycombing
- Lower lobe volume loss
  - –in emphysematous pt volume loss may be absent
- Whenever long standing reticulation with a lower lobe and peripheral preference is seen also think of ‘UIP’
- Occasionally CXR may be normal

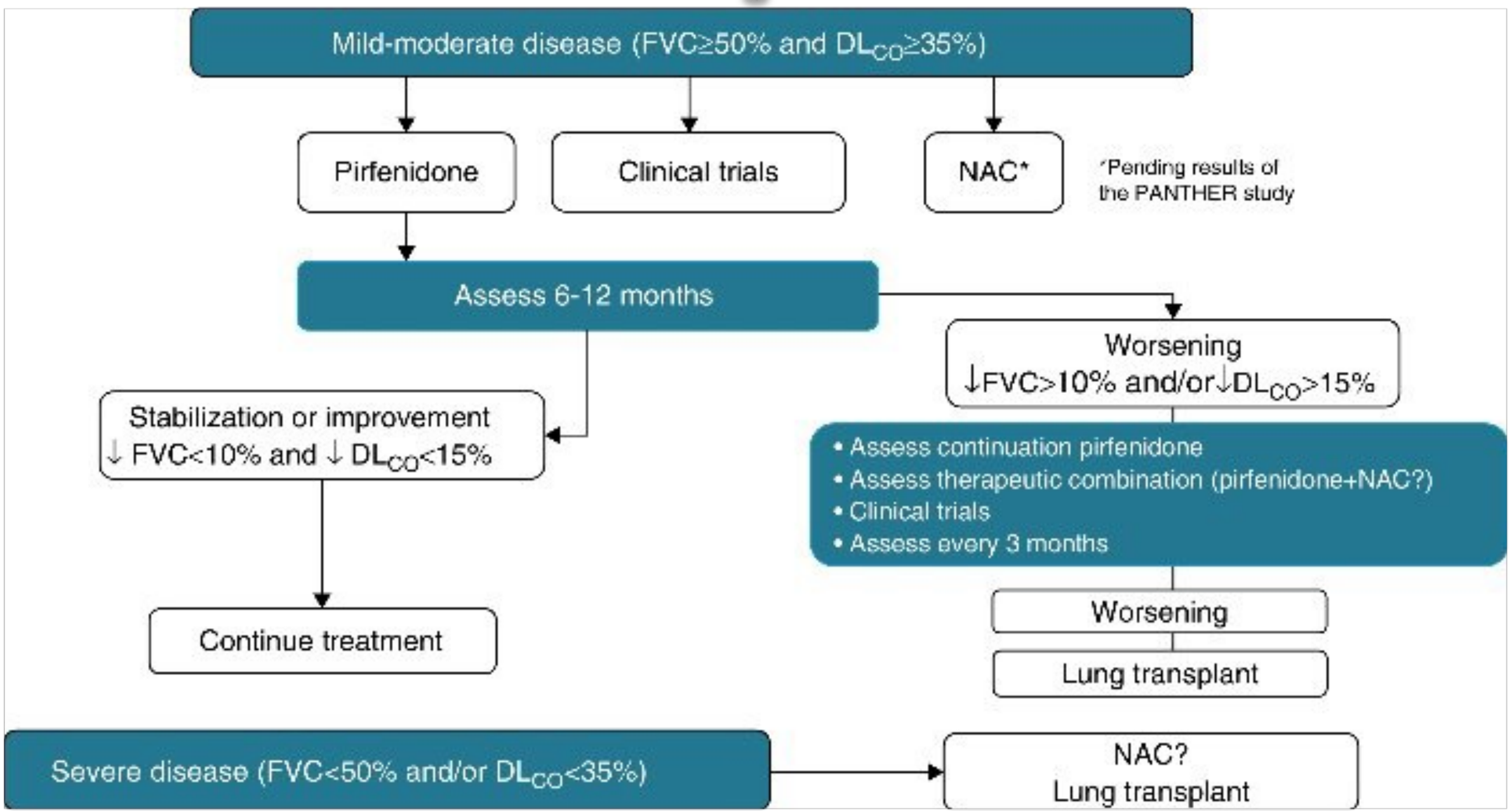

Suspected IPF
Other fibrosing lung diseases
Yes
No
HRCT
Clear UIP radiological pattern
Yes
Posible UIP Not consistent with UIP
Histology: clear UIP pattern
Yes
Surgical lung biopsy
Other DILD
Histology: Probable UIP Possible UIP Non-classifiable DILD
Yes
Multidisciplinary discussion
IPF
IPF/not IPF
Not IPF

management

- General
  - Oxygen therapy
    - For patients with documented hypoxia
      - SpO_2 < 89%
      - PaO_2 < 55 mmHg
    - Improves exercise tolerance
  - Adequate nutrition
  - Immunizations (pneumococcal, influenza)
  - Pulmonary rehabilitation
  - Treatment of PHT
  - Single-lung transplantation is a viable option

- Pirfenidone (antifibrotic)
  - –Reduces acute exacerbations and reduction in FVC

- N-acetyl cystein (antioxydant)
  N Engl J Med 2005;353:2229-42
  - –NAC 600 mg PO tid added to prednisone and azathioprine, preserves vital capacity and FVC and DLCO


Mild-moderate disease (FVC≥50% and DL_{CO}≥35%)
Pirfenidone
Clinical trials
NAC*
*Pending results of the PANTHER study
Assess 6-12 months
Stabilization or improvement
↓ FVC<10% and ↓ DL_{CO}<15%
Continue treatment
Worsening
↓FVC>10% and/or↓DL_{CO}>15%
• Assess continuation pirfenidone
• Assess therapeutic combination (pirfenidone+NAC?)
• Clinical trials
• Assess every 3 months
Worsening
Lung transplant
Severe disease (FVC<50% and/or DL_{CO}<35%)
NAC?
Lung transplant

Clinical diagnosis / Histo.	Clinically	CXR	B A L	HRCT findings / HRCT distribution	Treatment
IPF/CFA – UIP	65 yrs M:F =3:2 Insidious	Reticular ops, loss of volume > Basal	N	Reticular honeycombing, traction b'ectasis, focal GGO (rare) Peripheral, subpleural, basal	Steroids + Aza + N AC V poor prognosis Median Survival 3yrs
NSIP – NSIP	50-55yrs M:F =1:1 Insidious	GGO, reticular op	N, L	GGO, consolidation, reticular changes, honeycombing (rare) Peripheral, subpleural, basal, symmetrical	≈ to IPF Intermediate Prognosis Median Survival 6-7yrs
COP – OP - Buds of fibroproliferative tissue in alv. spaces	55 yrs M:F =1:1 Subacute	Consolidation – B/L patchy	N	B/L multifocal consolidation, GGO, nodules Subpleural, peribronchial	Steroids Good response

AIP – DAD	50 yrs M:F =1:1 Acute onset (≈ARDS)	GGO / consolidation – diffuse, progressive	Diffuse consolidation, GGO, with lobular sparing Diffuse BAL - L	No proven Rx IV Methylpred: Cyclophos Very poor prognosis Die < 6/12
DIP – Extensive accum of m'ph in intra-alveolar spaces	40-50 yrs M:F =2:1 Insidious. Exclusively in Smokers	GGO	GGO, reticular lines, centrilobular nodules Subpleural, basal	Better response to smoking cessation and systemic steroids than IPF Good prognosis
RB-ILD – RB Accum. of m'ph in peribronc alveoli	40-50 yrs M:F =2:1 Insidious. Smoking related	Bronchial wall thickening, GGO	Bronchial wall thickening, centrilobular nodules, patchy GGO Diffuse	Resolve with smoking cessation alone in most cases Good prognosis
LIP – LIP	40-50 yrs M:F =1:5 Insidious	Reticular ops, nodules	Centrilobular nodules, GGO, septal & bronchovascular thickening, thin walled cysts, L'adenopathy Diffuse	Intermediate prognosis