Interstitial Lung Diseases

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Definition

- a group of disease which predominantly affect the pulmonary connective tissue and interstitium (between the air sacs of the lungs) of the alveolar walls and share a common response of the lung to injury: alveolitis; inflammation; fibrosis of the interalveolar septum

- also known as“interstitial pulmonary fibrosis”or “diffuse parenchymal lung disease (DPLD)”

Common clinical feature

1. Exertional dyspnea or nonproductive cough
2. Tachypnea and bibasilar end-inspiratory dry cracks
3. Bilateral diffuse infiltrates on chest radiographs
4. Presents as a **RESTRICTIVE** lung disease, DLco↓, $P_{A\text{-}a}O_2$↑
5. Varying degrees of fibrosis and inflammation, with or without evidence of granulomatous or secondary vascular changes

What is the cause of ILD?

- >180 kinds
- Chief known cause (1/3)
  - Inhale inorganic dusts
  - Inhale organic dusts
  - Radio-active injury
  - Micro-organic infection
  - Drugs
  - Lymphocytic carcinoma
  - Pulmonary edema

What is the cause of ILD?

- **Chief unknown cause**
- **Primary lung diseases**
- **ILD associated with system disorder (CTDs)**
- **Alveolar filling disorder**
- **ILD associated with pulmonary vasculitis**
- **Inherited disorders**

Classfication-1

1.According to process: Acute/Subacute/Chronic

2. According to cause: Clear /Not clear

3. According to pathology

Granulomatous disease / non-tumor and non-inflammatory diseases / non-specific diseases / occupational diseases / hyperplastic and tumourous diseases / interstitial lung diseases and honey lung

Classfication-2 (According to pathology)

- **Interstitial lung Diseases**

1.usual interstitial pneumonia (UIP)
2.nonspecific interstitial pneumonia (NIP)
3. respiratory bronchiolitis (RB)
4. organizing pneumonia (BOOP)
5. diffuse alveolar damage
6. desquamative interstitial pneumonia (DIP)
7. lymphocytic interstitial pneumonia (LIP)

Pathogenesis

- The lung heals in a predictable, consistent manner
- Causes may differ but pathogenesis remains the same
  - Cause = insult, injury, infection, toxin, etc
  - Cause is what differentiates the individual diseases and their treatments
- leads to alveolitis→initial event in all interstitial lung diseases

Injury

- Alveolitis?- the presence of immune cells within the alveolar walls
- Immune cells
  - Secrete cytokines recruiting more immune cells and triggering complex chain of events called “inflammation”
  - Cause direct tissue injury
    - Generate oxygen free radicals
    - Release proteases

Pathogenesis

- Alveolar wall and tissue damage lead to leakage of a fibrin-rich exudate into the alveolar spaces

Pathogenesis - Key point

- Type I pneumocytes
  - Very susceptible to injury
  - Cannot regenerate
- Type II pneumocytes
  - More resistant to injury
  - Regenerate and differentiate into Type I pneumocytes
  - Proliferate in injury laying down a new epithelial layer

Pathogenesis

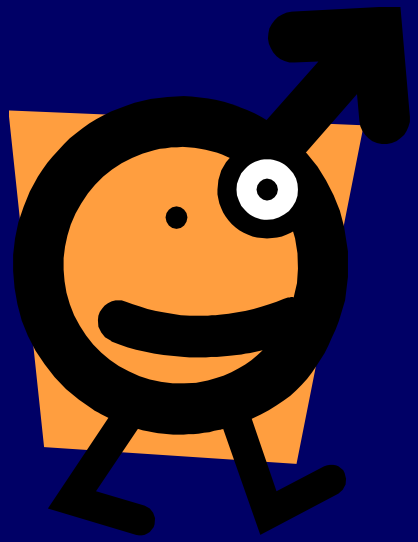
- **Fibroblasts migrate across the damaged alveolar wall into the alveolar space and into the fibrin-rich exudate**

- **Fibrin is organized, collagenized and covered by alveolar epithelium**

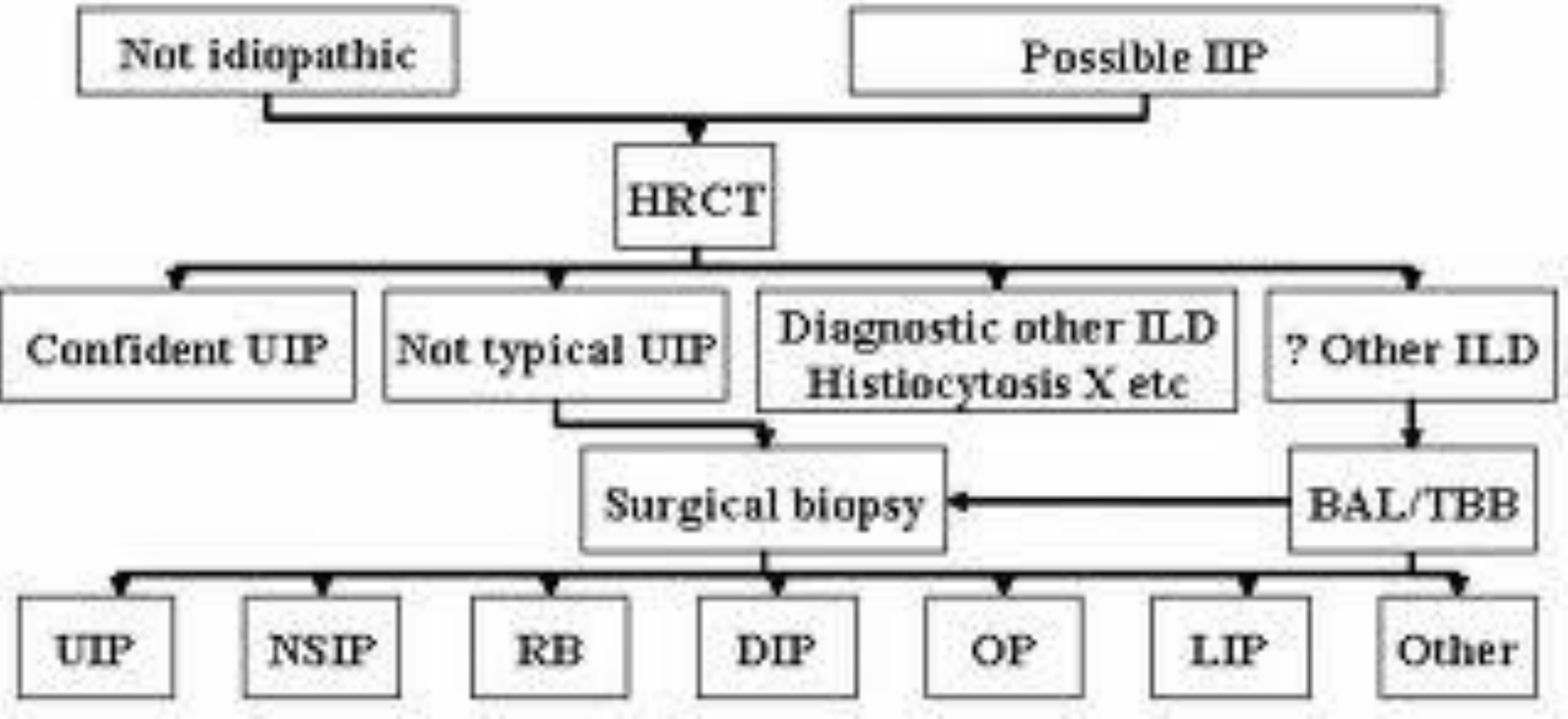
If the injury persists…

- Fibrosis continues, leading to obliteration of the delicate interstitium
- Normal lung architecture is distorted because fibrosis scars down “pulling” on bronchiolar spaces causing dilatation and a cyst-like architecture
- Final stage is referred to as End Stage Lung or Honey Comb Lung

How to make a diagnosis?



Diagnostic path

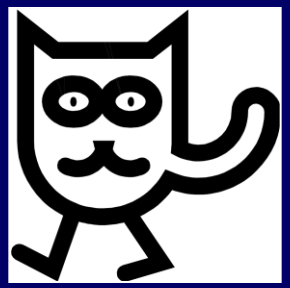


Diagnostic Tests Used for Identification

1. **Blood Tests**
2. **Pulmonary Function Tests**
3. **Chest X-ray**
4. **CT Scan**
5. **Bronchoscopy : TBLB or BAL**
6. **Lung Biopsy : TBLB or OLB or TGLB**

Pulmonary Function Tests

- Restrictive pattern
  - ↓ lung volume
  - ↓ compliance
  - ↓ diffusing capacity
  - Thus
    - ↓ FVC
    - ↓ FEV1
    - ↓ TLC
    - ↓ DLco
    - But, NORMAL FEV1/ FVC ratio



Chest imaging studies

- X-ray
  - Diffuse reticular infiltrates, micronodular
- CT scan
  - Fine to coarse reticular or reticulonodular infiltrates, lung fibrosis and honeycomb
  - Peripheral ground- glass opacities

Bronchoalveolar lavage (BAL)

-to make a diagnosis ,differential diagnosis, treatment

-to exclude infections and malignancies (cancer)

-to identify inflammation in lung tissue

Lung biopsy

1. Bronchoscopy (TBLB)

   20-40%(+), to diagnosis of sarcoidosis – 80%

2. Open-lung biopsy (OLB)

3. Thoracoscopy-guide lung biopsy (TGLB)

Idiopathic pulmonary fibrosis (IPF)

Alao named as cryptogenic fibrosing alveolitis, chronic inflammation of the alveolar walls with progressive fibrosis, of unknown etiology

IPF - Epdemiology

- Age ：40s - 50s
- Male to female ratio 2/1 (1/1)
- Prevalence: 5/100,000

Usual interstitial pneumonia (UIP) (IPF)

Histologic findings

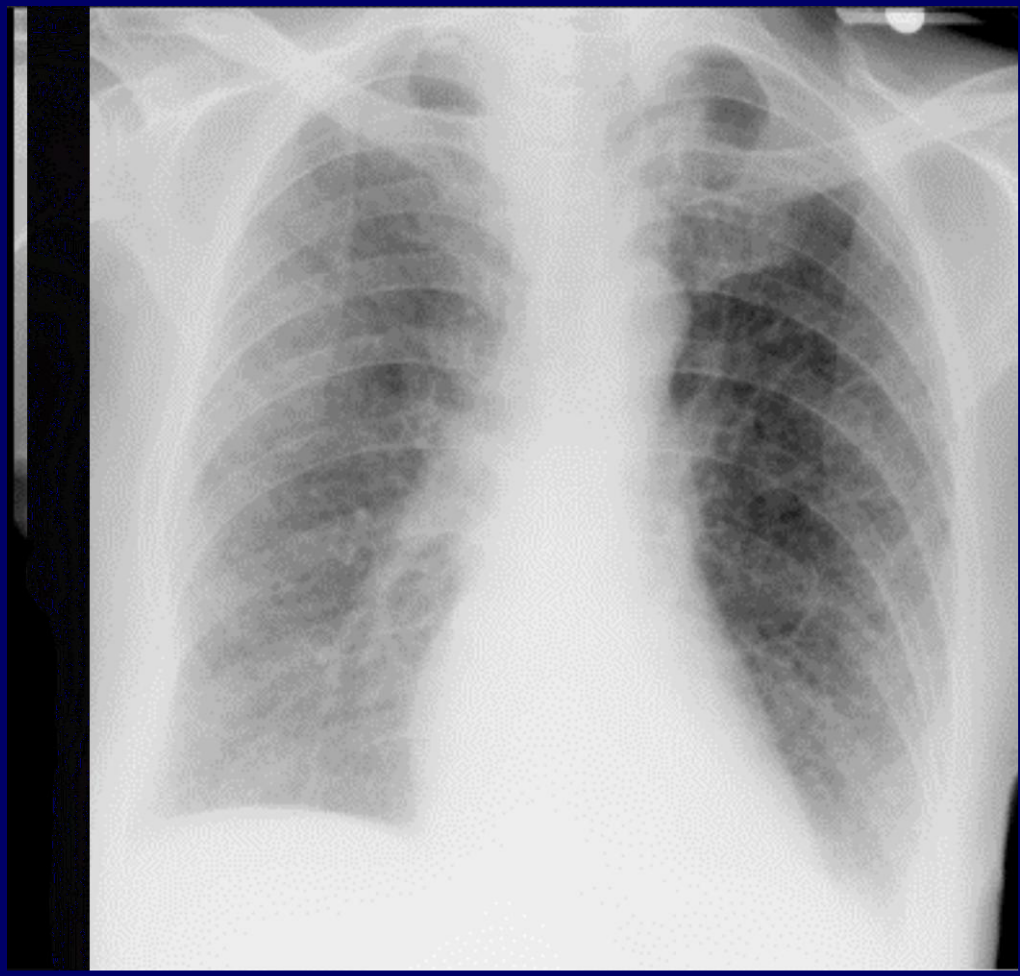
1) **dense fibrosis with remodeling of lung architecture with honeycomb change**
2) **fibroblastic foci & fibrotic zones with temporal heterogeneity**
3) **Smooth muscle hyperplasia in areas of fibrosis**
4) **in septa and beneath the pleura.**
5) **patchy lung involvement**

Symptoms and Signs

- **Symptoms**
  - **dyspnea on exertion, Progression over months,**
  - **nonproductive cough**
- **Physical Examination**
  - **tachypnea**
  - **clear lungs or “velcro” rales (inspiratory crackles)**
  - **signs of pulmonary hypertension (Incr. P_2, cor pulmonale)**
  - **digital clubbing and cyanosis**

Radiography exam.

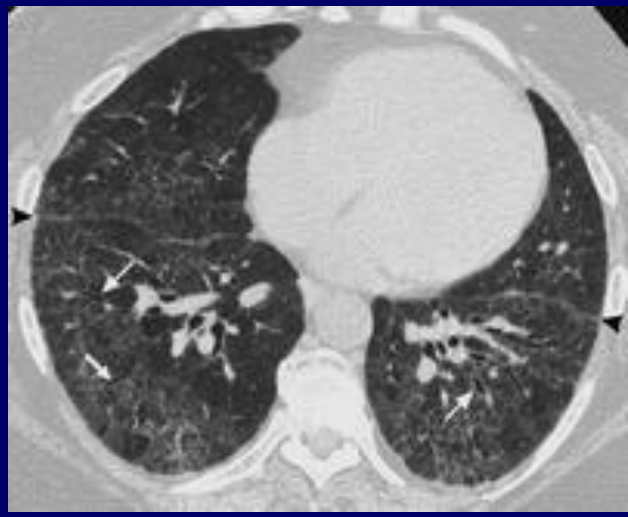
- **CXRs: lower zones, interstitial, ground glass, honey combing**

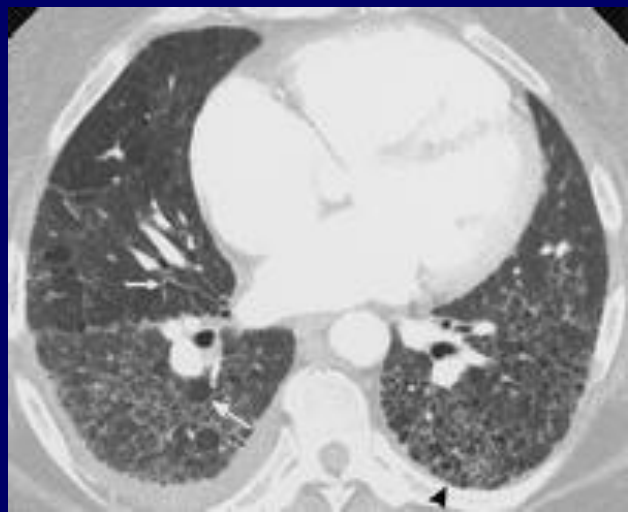


Usual interstitial pneumonia (UIP) (IPF)

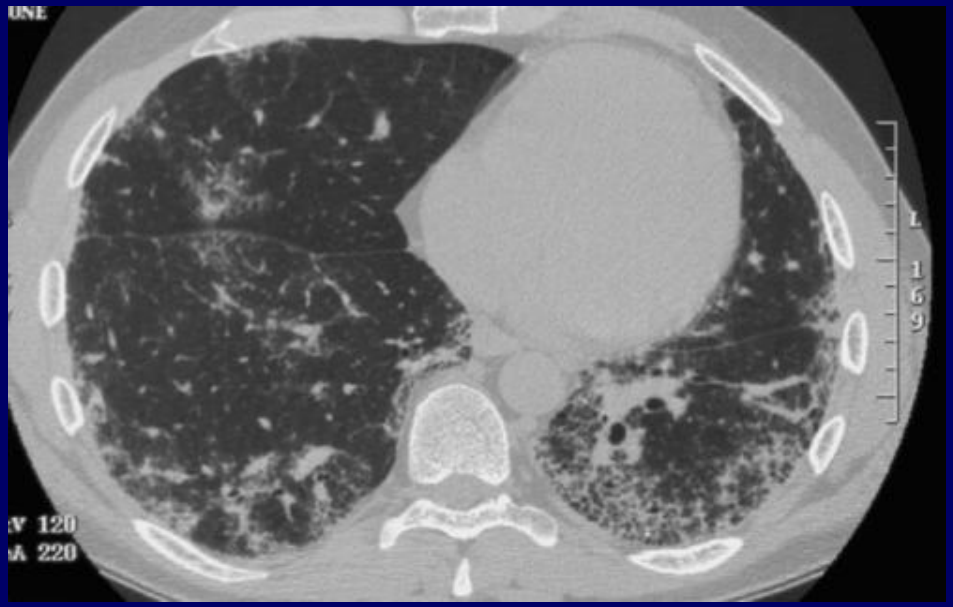
CT Features

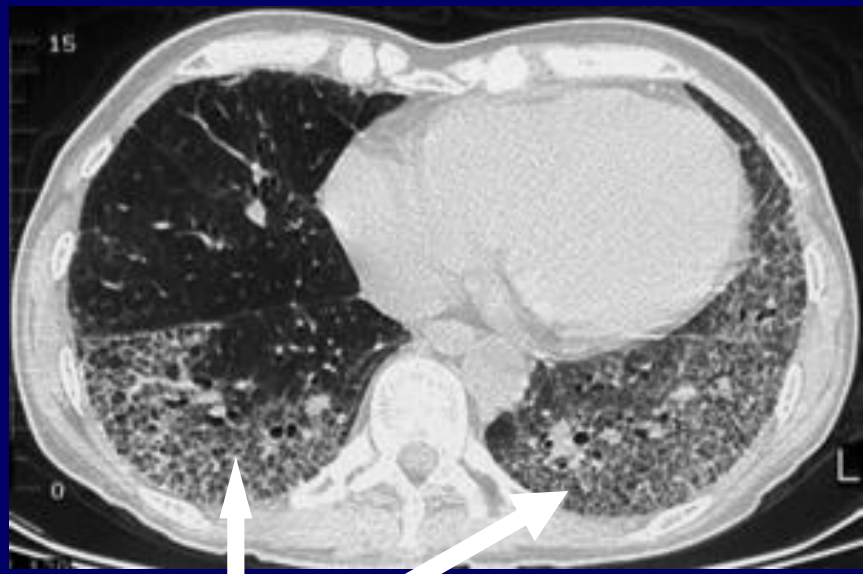
1) reticular attenuation with lobular septal thickening
2) architectural distortion
3) honeycomb pattern
4) ground-glass attenuation
5) predominantly basal & peripheral in distribution





Idiopathic pulmonary fibrosis
- High resolution CT





diffuse, patchy, subpleural, reticular opacities with irregularly thickened interlobular septa and intralobular lines and subpleural honeycombing

IPF -- Labs

- PFTs: Restrictive
- Hypoxemia:
- first with exercise
  - later at rest
- LDH, γ-Globulin↑; RF +
- ANA can be (+)
- lung biopsy: open or video-assisted thoracoscopic; not indicated when x-rays show extensive honeycombing

Diagnosis

- Clinical features and lab findings
- Exclude other kind of ILD

Treatment

(1)Prednisone: 1.0 mg/kg/d, 3 mo

taper to 0.5 mg/kg (5mg/week,3 mo)

0.25 mg/kg or 15-20mg/d (the next 6 mo)

(2)Cytotoxic drugs: cyclophosphamide / azathioprine, 1-2 mg/kg/day

(3)New: Perfenidone, interferon g

Treatment

(4) Supportive : O2 , treat infections, etc.

(5) Lung transplantation: end-stage

(6) Rehabilitation and education programs

Prognosis

- **Poor - mean survival is 4 years;**

  median survival: 4 - 6 yr after diagnosis
- **Worse if > 10% PMNs + Eos. on BAL**
- **Better if lymphocytes on BAL**
- **Histology: DIP**

Sarcoidosis

- Chronic multisystem disorder of unknown cause characterized in affected organs by an accumulation of T lymphocytes, noncaseating epithelioid granulomas and derangements of the normal tissue architecture

Etiology

- **Unknown**

- **Exaggerated celluar immune response (acquired, inherited or both)**

Incidence and Prevalence

- All ages, most between the ages of 20 and 40
- Both sexes, female slightly more susceptible than males

Symptoms and Signs

- **Acute or subacute (20%-40%)**

  fever, fatigue,malaise,anorexia,weight loss

  cough, dyspnea, a vague retrosternal chest discomfort, and /or polyarthritis

Symptoms and Signs

Lung

- **Primarily an interstitial lung disease**
- **Distal atelectasis**
- **Large-vessel pulmonary granulomatous arteritis**

Lymph node

- **Lymphadenopathy is very common**
- **Intratharacic nodes are enlarged—75%-90%**

Complication

- Respiratory tract abnormalities---morbility and mortality
- Eye
- Central nervous system---most serious

Larboratory Abnormalities

- ACE
- Graph

type I—bilateral hilar adenopathy acute subacute

type II--with diffuse parechymal changes chronic

type III-- diffuse parechymal changes chronic

Diagnosis

- Clinical features and lab findings
- Exclude other kind of noncaseating granulomas

Prognosis

- Overall is good
- Most acute disease with no significant sequelae
- 50% have some permanent organ dysfunction---most is mild,stable
- 15%-20%----active or recurs intermittently

Treatment

- Glucocorticoids
- Methotrexate
- Other drugs

when to treat?

Treatment

- **Prednisone: 1.0 mg/kg/d, 4 mo -6mo**

  Slow taper over 2 to 3

- **Methotrexate: 5 to 15 mg/week in a single oral dose when glucocorticoids are contraindicated or in refractory cases**

- **Lung transplant-------end-stage**

Question?

- What are the Common clinical features ?
- What can we find from pulmonary function test ?
- How to make a diagnosis?