"He who studies medicine without books sails an uncharted sea, but he who studies medicine without patients does not go to sea at all."
William Osler

Medicine

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Diffuse Parenchymal Lung Disease
(Interstitial Lung Disease)

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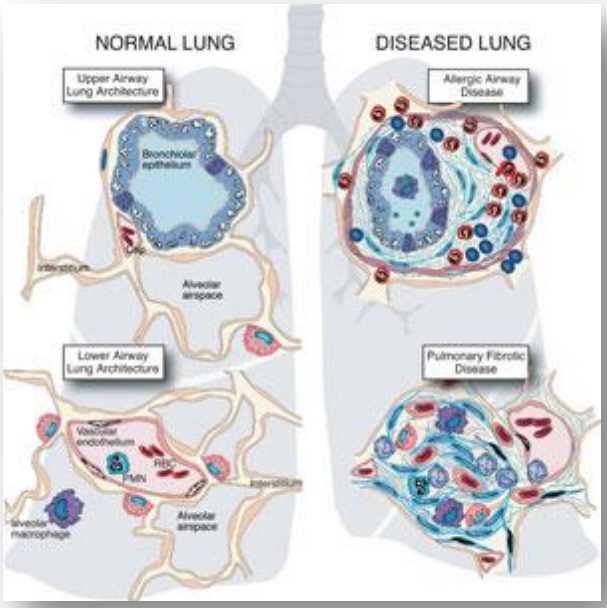
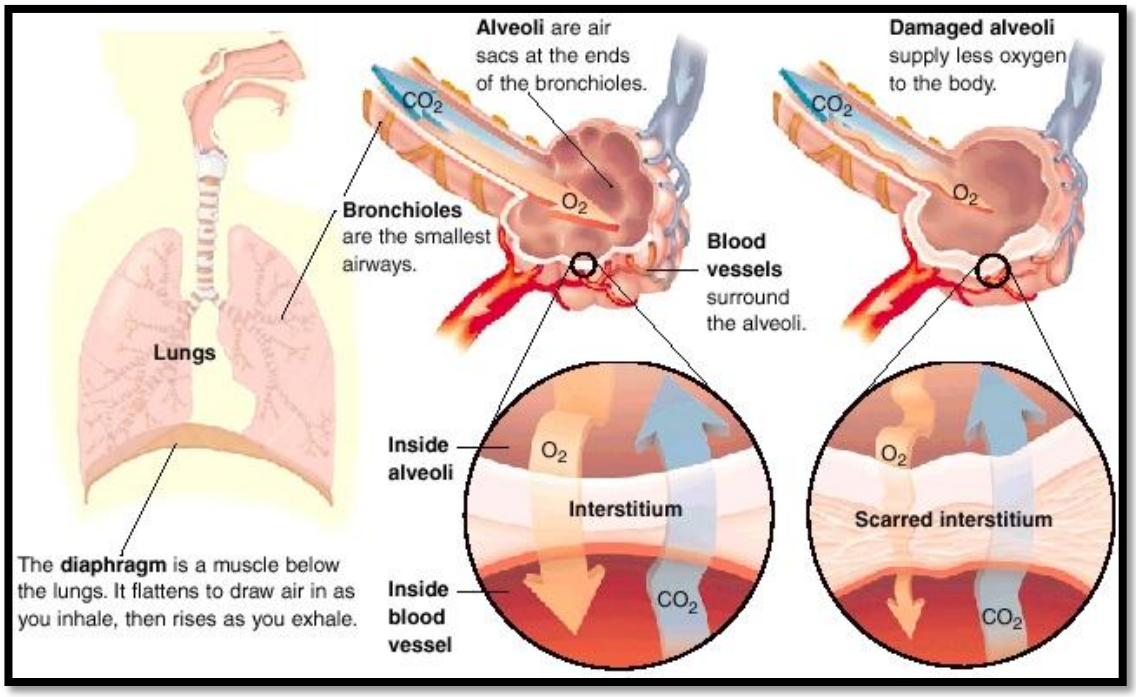
Defuse Parenchymal Lung Disease (Interstitial Lung Disease)

Definition:

- Defuse parenchymal lung disease (Interstitial lung disease)
- Are a heterogeneous group of disorders associated with injury to the pulmonary parenchyma, leading to chronic interstitial inflammation, then to fibroblast activation and proliferation and finally progressing to pulmonary fibrosis and tissue destruction.





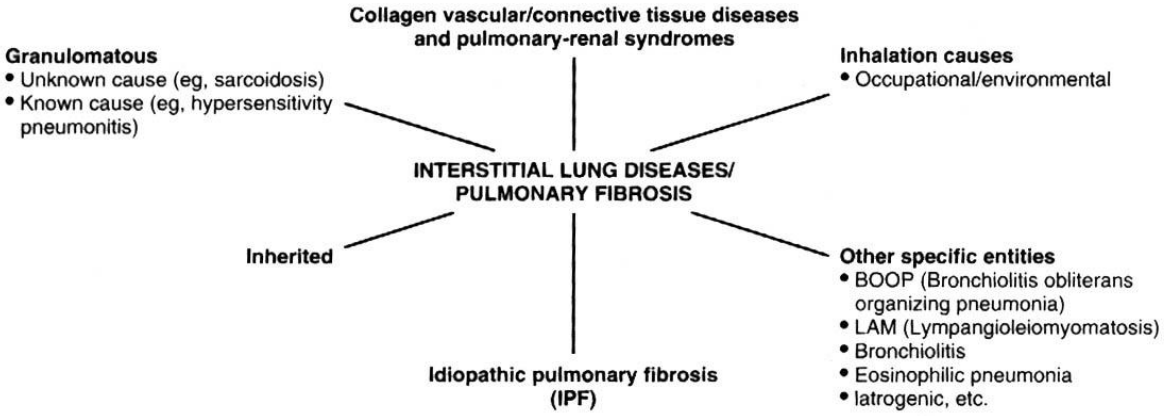


Figure 7–24. Categories of interstitial lung disease. In the absence of underlying malignancy or history of chemical or radiation therapy, interstitial lung disease can be broadly grouped into the clinical categories shown. Idiopathic pulmonary fibrosis occurs in a majority of these patients. (Reproduced, with permission, from Raghu G, Hert R: Interstitial lung diseases: Genetic predisposition and inherited interstitial lung diseases. Semin Respir Med 1993;14:323.)

Classification:

1. Acute
2. Episodic (may present acutely)
3. Chronic due to occupational, environmental agents or drugs
4. Chronic with evidence of systemic disease
5. Chronic with no evidence of systemic disease

Or

1. Idiopathic
2. Non idiopathic

Non idiopathic DPLD

Environmental or occupational exposures

- Pneumoconiosis
    - (Inhalational exposures to inorganic dusts e.g. silicosis, asbestosis, berylliosis, coal worker's pneumoconiosis)
- Hypersensitivity pneumonitis (HSP)
    - Caused by exposure to protein antigens (e.g., farmer's lung, pigeon-breeder's lung)
    - Fibrotic lung disease due to exposure to toxic gases, fumes, aerosols, and vapors (e.g., silo-filler's disease)
- Radiation exposure

Connective-tissue diseases

- Scleroderma (progressive systemic scleroderma) (CREST syndrome)
- Rheumatoid arthritis
- Mixed connective-tissue disease
- Systemic lupus erythematosus
- The pulmonary-renal syndromes
    - Wegner or Goodpasture disease
    - Predominant manifestation is vasculitis rather than fibrosis

Drug exposure

- Cytotoxic agents (Bleomycin, busulfan, methotrexate)
- Antibiotics (Nitrofurantoin, sulfasalazine)
- Antiarrhythmics (Amiodarone, tocainide)
- Anti-inflammatory (Gold, penicillamine)
- Illicit drugs (Crack cocaine, heroin)

Unknown causes

- Sarcoidosis & other granulomatous diseases

Related to other systemic illnesses

- Hepatitis C
- Inflammatory bowel disease
- Acquired immunodeficiency syndrome (AIDS)

Inherited

- Familial IPF or sarcoidosis
- Tuberous sclerosis
- Neurofibromatosis
- Gaucher disease

Idiopathic interstitial pneumonia

- Idiopathic pulmonary fibrosis (IPF)

Or

- Idiopathic interstitial pneumonia (other than IPF)
    - Desquamative interstitial pneumonia
    - Acute interstitial pneumonia
    - Respiratory bronchiolitis interstitial lung disease
    - Non-specific interstitial pneumonia
    - Cryptogenic organizing pneumonia (COP)
    - Lymphocytic interstitial pneumonia

Idiopathic pulmonary fibrosis

- (IPF) is an idiopathic interstitial pneumonia that is characterized histopathologically by the presence of usual interstitial pneumonia.
- It Is the most common idiopathic pulmonary fibrosis portends a poor prognosis
- Males > females aged 50 -70 years or older

Clinical features:

- Gradual onset dyspnea (At first with exertion, later at rest)
- Nonproductive cough
- Systemic symptoms (not common)
- Weight loss, low-grade fevers, fatigue, arthralgias, or myalgias
- O/E Fine bibasilar inspiratory crackles (Rales at the bases are commom)
    - Digital clubbing in 25-50% of patients (Especially with IPF)

Signs of pulmonary HTN and cyanosis in advanced disease

Pathophysiology

- Generalized inflammation progressed to widespread parenchymal fibrosis
- It Is an epithelial-fibroblastic disease
- Unknown
- Endogenous or environmental stimuli disrupt the homeostasis of alveolar epithelial cells
- Diffuse epithelial cell activation and aberrant epithelial cell repair

Activated alveolar epithelial cells → release potent fibrogenic cytokines and growth factors: tumor necrosis factor-α (TNF-α), transforming growth factor-β(TGF-β) platelet-derived growth factor, insulin like growth factor-1 and endothelin-1 (ET-1)

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migration and proliferation of fibroblasts and the transformation of fibroblasts into myofibroblasts

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fibrogenesis, and myofibroblasts secrete extracellular matrix proteins. (myofibroblasts must undergo **apoptosis**)

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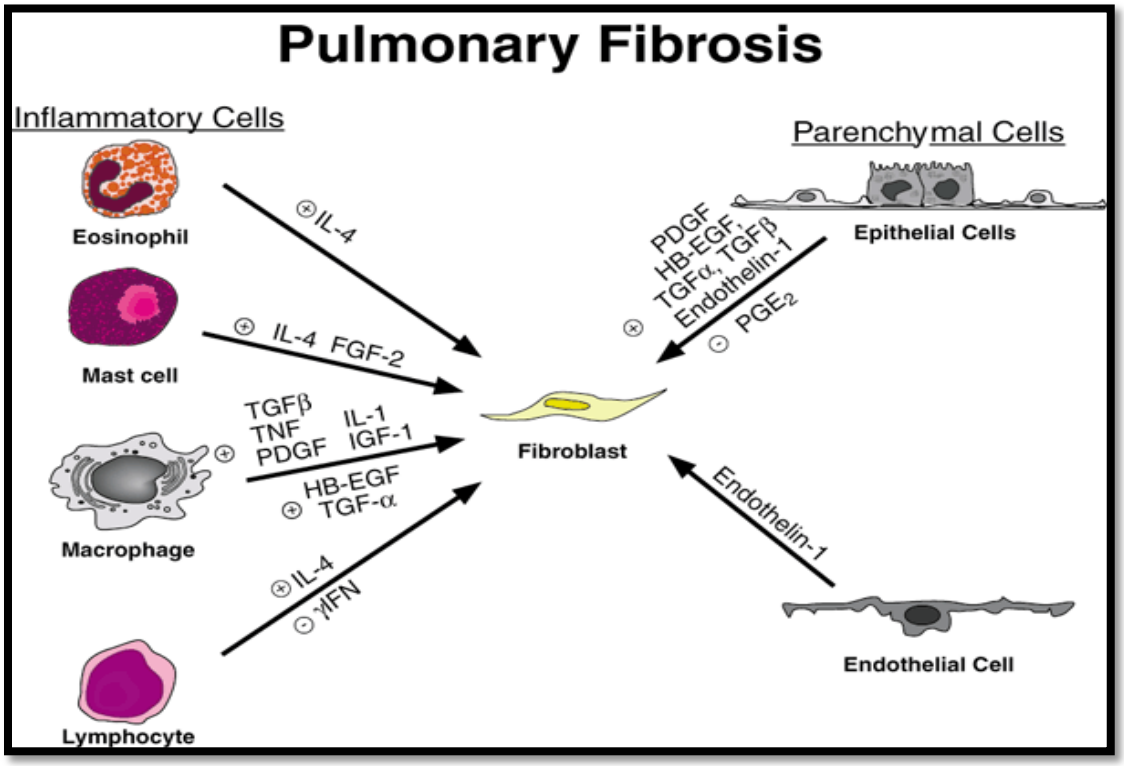
- Failure of apoptosis leads to myofibroblast accumulation
- Exaggerated extracellular matrix protein production
- persistent tissue contraction, and pathologic scar formation.

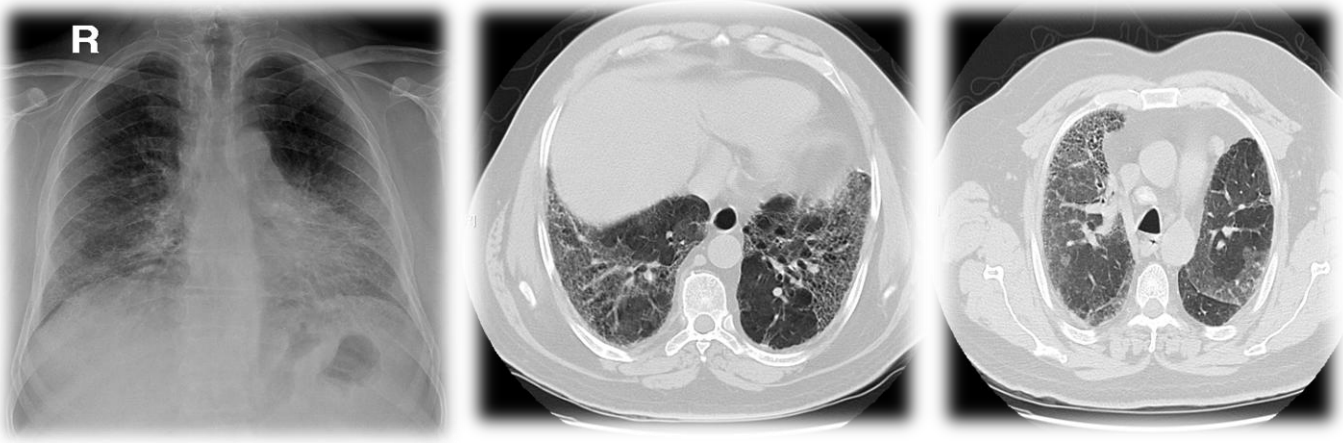


Work Up

- History (job, smoking ,hobbies , pets & drugs)
- Clinical exam

Investigations

- CXR
    - Findings are usually nonspecific
    - Typical diffuse changes are noted (reticular, riticulonodular, ground glass, honeycombing)
- Full blood count, CRP and ESR and U&Es
- Liver function
- ANA and rheumatoid factor
- Autoantibodies , Serum precipitins
- ANCA/anti- GBM
- ACE
- Lung function tests (VC/TLCO), 6 MWD
    - A restrictive pattern is noted: FEV1/FCV ratio is increased
    - All lung volumes are low
    - Both FEV1 and FCV are low but the later more so
    - Low diffusing lung capacity (DLCO)
- ECG/echocardiography
- HRCT
    - High Resolution CT Scan shows the extent of fibrosis better than other imaging modalities.
- Bronchoscopy to do ;transbronchial biopsy
- Broncho alveolar lavage (BAL)
    - Fluid for culture and cytology – Use is controversial because results are quite variable
- Video-assisted thoracoscopy/open lung biopsy
    - Biopsy is often required in patients with ILD
- Urinalysis, if there are signs of glomerular injury (for Goodpasture's syndrome and Wegner's granulomatosis)



Treatment

- There is no known medical therapy proven to have enhanced survival and improved outcomes for patients with IPF
- Treatment of comorbid medical condition
- Current smoker should be encouraged to quit
- Treat associated GERD
- Vaccination against influenza and pneumococcal infection
- Supportive measures
- Supplemental oxygen therapy
- Palliation of breathlessness
- ‘‘untreatable’’ cough oral opiates can be used
- Treat PAH
- Smoking cessation
- Rehabilitation
- Nutrition (BMI) of (17 and .27 kg m-2)

Corticosteroids

- Symptomatic improvement
- Is an appropriate treatment option for acute exacerbation

In the past

- Immunosuppressant
- Cyclophosphamide
- Azathioprine
- Treble treatment
- N-acetylcysteine (NAC) an antioxidant together with corticosteroids in combination with other immunosuppressive drugs such as azathioprine
- Antioxidants N -acetylcysteine (NAC)
- Azathioprine and oral corticosteroids and/or NAC
- Biological response modulators
- Etanercept, recombinant s human TNF receptor
- Interferon-γ
- Endothelin receptor antagonistsPhosphodiesterase inhibitors

Promising treatment

- Tyrosine kinase inhibitors
- Antifibrotic agents
- Pirfenidone, a novel compound with combined anti-inflammatory, antioxidant, and antifibrotic effects, had potential therapeutic benefits for idiopathic pulmonary fibrosis

Surgical Care

- Patients at increased risk of mortality should be considered for lung transplantation
- Life threatening disease despite optimal medical treatment.

Transplantation

When should patients be referred?

- Life threatening disease despite optimal medical treatment.
- A diffusion capacity of carbon monoxide (DL_{CO}) less than 39% predicted
- A 10% or greater decrement in forced vital capacity during 6 months of follow-up
- A decrease in pulse oximetry below 88% during a 6-minute walk test (6MWT),
- + Resting hypoxia
- + Pulmonary hypertension

Which patients should be referred?

- 60 years old
- Discuses physically robust patients up to 65 years with the transplant center

Reference:

Step Up To Medicine , Second Edition