Medicine Team Notes

Diffuse Parenchymal Lung Disease

429 Medicine Team

ABSTRACT

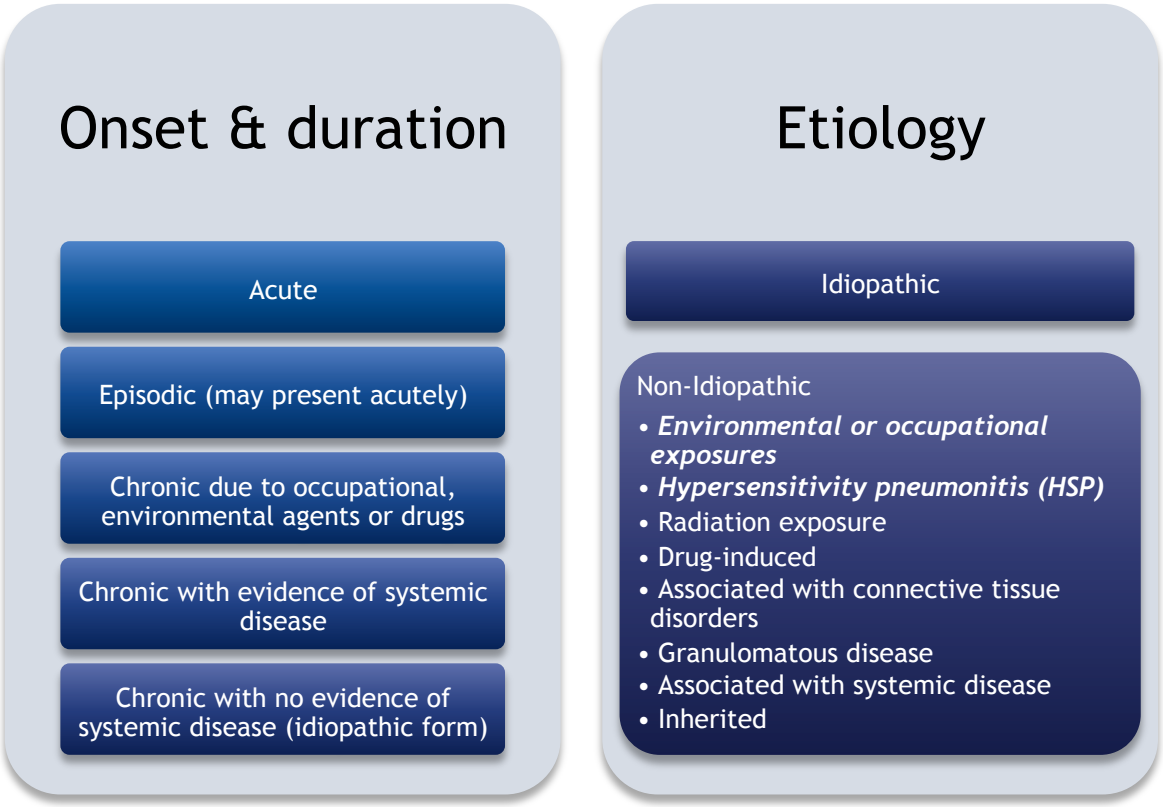
These notes include the doctor’s comments during the lecture in addition to notes from Kumar and Clark's Clinical Medicine 7e, and Step-Up to Medicine 2e

DEFINITION

Defuse parenchymal lung disease (Interstitial lung disease):

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.

CLASSIFICATION



NON-IDIOPATHIC

1. Environmental/Occupational Exposures

a. Pneumoconiosis: due to inhalation of inorganic dusts
   i. Asbestosis
   ii. Silicosis: mining, stone-cutting & glass manufacturing
   iii. Coal worker's pneumoconiosis: inhalation of coal dust (carbon + silica)
   iv. Beryllosis: massive exposure to beryllium

b. Hypersensitivity pneumonitis
   i. Caused by exposure to protein antigens (e.g., farmer's lung: exposure to moldy hay, pigeon-breeder's lung: exposure to avian droppings)
   ii. Fibrotic lung disease due to exposure to toxic gases, fumes, aerosols, and vapors (e.g., silo-filler's disease: exposure to oxides of nitrogen)

c. Radiation exposure

2. **Connective Tissue Diseases**
    a. Scleroderma (progressive systemic scleroderma) (CREST syndrome)
    b. Rheumatoid arthritis
    c. Mixed connective-tissue disease
    d. Systemic lupus erythematosus
    e. The pulmonary-renal syndromes (Wegner's; granulomatous or Goodpasture's disease; autoimmune, alveolar filling disease)
        i. Predominant manifestation is vasculitis rather than fibrosis
3. **Drug Exposure**
    a. *Cytotoxic agents* (Bleomycin, busulfan, methotrexate)
    b. *Antibiotics* (Nitrofurantoin, sulfasalazine)
    c. *Antiarrhythmics* (Amiodarone, tocainide)
    d. *Anti-inflammatory* (Gold, penicillamine)
    e. *Illicit drugs* (Crack cocaine, heroin)
4. **Sarcoidosis & other granulomatous diseases** e.g. Histocytosis X, Wegener's granulomatosis, Churg-Strauss syndrome
5. **Other systemic illnesses**
    a. Hepatitis C
    b. Inflammatory bowel disease
    c. Acquired immunodeficiency syndrome
6. **Inherited**
    a. Familial IPF or sarcoidosis
    b. Tuberous sclerosis
    c. Neurofibromatosis
    d. Gaucher disease: glucocerebrosidase deficiency; genetic disease in which lipids accumulates in cells and organs

IDIOPATHIC

1. IDIOPATHIC PULMONARY FIBROSIS (IPF)

- Characterized histopathologically by the presence of usual interstitial pneumonia
- Is the most common idiopathic pulmonary fibrosis portends a poor prognosis
- Males > females, aged 50 -70 years or older

2. 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

CLINICAL FEATURES

SYMPTOMS

- Gradual onset dyspnea (at first with exertion, later with rest)
- Nonproductive cough
- Systemic symptoms (not common.)
- Weight loss, low-grade fevers, fatigue, arthralgias, or myalgias

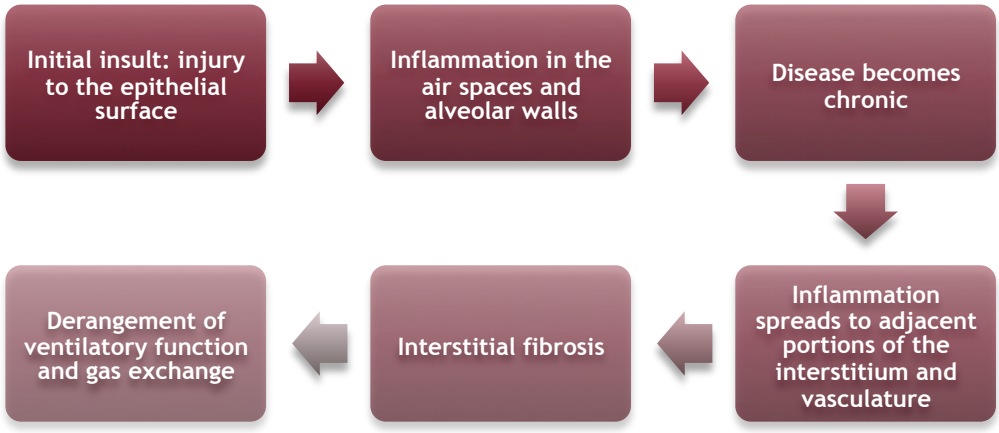
Symptoms are PROGRESSIVE

SIGNS

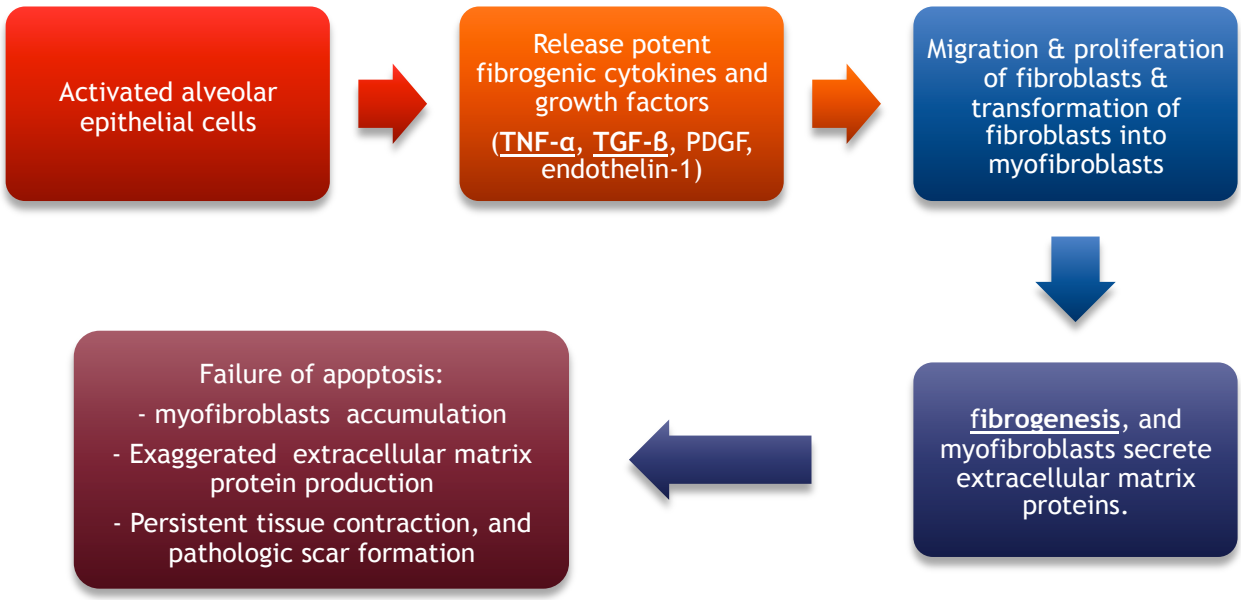
- Fine bibasilar inspiratory crackles
- Digital clubbing in 25-50% of patients (because of chronic hypoxia)

PATHOPHYSIOLOGY

- Generalized inflammation progressed to widespread parenchymal fibrosis
- 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



PATHOPHYSIOLOGY ON A CELLULAR LEVE



INVESTIGATIONS

HISTORY

Occupation (previous), smoking, hobbies, pets & drugs

LAB TESTS

- CXR:
    - Most cases: non-specific findings
    - Commonly: bibasilar reticular pattern
    - A subgroup of ILDs exhibit nodular opacities with a predilection for the upper lung zones [sarcoidosis, PLCH, chronic hypersensitivity pneumonitis, silicosis, berylliosis, RA (necrobiotic nodular form), ankylosing spondylitis]
    - Honeycombing correlates with pathologic findings of small cystic spaces and progressive fibrosis; when present, it portends a poor prognosis
- Full blood count, CRP (C-Reactive Protein) and ESR (Erythrocyte Sedimentation Rate) and U&Es (Urea & Electrolytes)
    - Elevated in inflammatory conditions
- Liver function (elevated e.g. in SLE)
- Serum precipitins (raised IgE) in hypersensitivities e.g. Farmer's lung
- Autoantibodies
    - Anti-GBM: Goodpasture's
    - c-ANCA (anti-neutrophilic cytoplasmic antibodies): Wegener's
    - p-ANCA (peri-nuclear anti-neutrophilic cytoplasmic antibodies): Goodpasture's, Churg-Strauss
    - Anti-Nuclear Antibodies (SLE)

    - Rheumatoid factor
- ACE: elevated in sarcoidosis
- Lung function tests (↓ VC/TLCO)
    - Restrictive ventilatory defect - the lung volumes are reduced, the FEV_1 to FVC ratio is normal to high (with both values being reduced), and carbon monoxide gas transfer is reduced. Peak flow rates may be normal
- 6-Minute Walk Test: The goal is for the individual to walk as far as possible in six minutes
- ECG/echocardiography (signs of pericarditis with connective tissue disorders e.g. SLE)
- HRCT: better assessment of the extent and distribution of disease
- Biopsy:
    - Bronchoscopy: transbronchial biopsy
    - *Video-assisted thoracoscopy/open lung biopsy*
- Bronchoalveolar lavage (BAL)

TREATMENT

SUPPORTIVE MEASURES

- Supplemental oxygen therapy
- Palliation of breathlessness; "Untreatable" cough: oral opiates can be used
- Treat pulmonary arterial hypertension
- Smoking cessation
- Rehabilitation
- Weight modification: Proper nutrition (BMI) of (17 and .27 kg/m^2)

DRUGS

CORTICOSTEROIDS

- Symptomatic improvement (50%)
- Objective improvement, defined as an increase in FVC of 10% and TLCO 25%
- Steroid response is associated with better survival

CYCLOPHOSPHAMIDE

- Not effective alone
- Side effects are common
- Response may take several months to become evident

AZATHIOPRINE

- Survival benefit when added prednisolone
- Side effects were not a problem

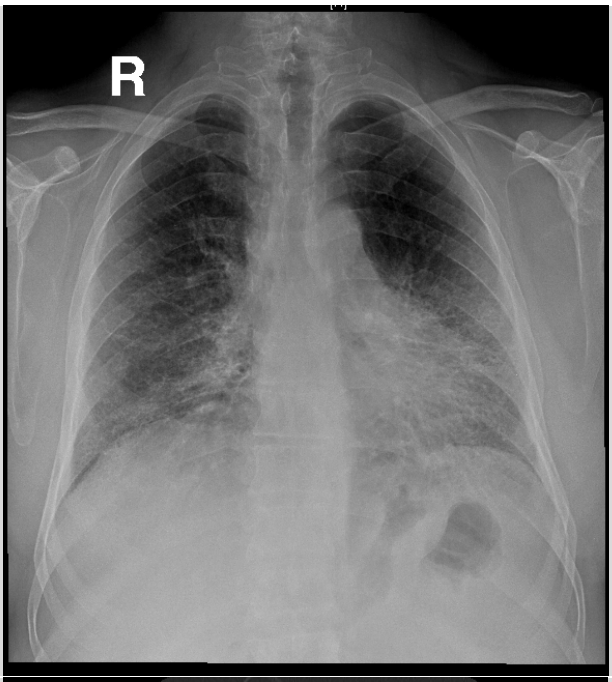
N-ACETYLCYSTEINE

- An antioxidant
- Used together with corticosteroids in combination with other immuno-suppressive drugs such as azathioprine
- Slows the deterioration of vital capacity and single-breath diffusing capacity

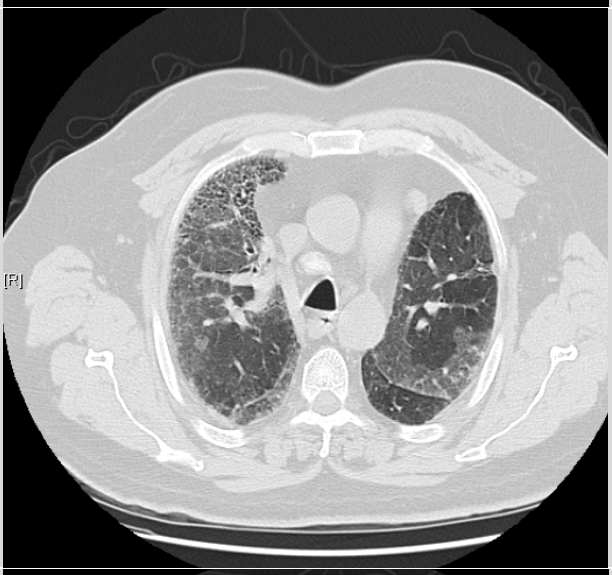
TRANSPLANTATION

WHEN SHOULD PATIENTS BE REFERRED?

- Life threatening disease despite optimal medical treatment
- Failed trial of corticosteroid therapy
- TLCO and/or VC below 50–60%
- Resting hypoxia
- Pulmonary hypertension
- Below 60 years old
- Physically robust (fit) patients up to 65 years



Chest X-Ray:
Reduced volume, reticulation & fibrous tissue



HRCT:
Ground-glass appearance
Honeycombing (usually around the pleura)
Patchy (not generalized)