Interstitial Lung Diseases

RSPT 2310

Pneumoconiosis

- Interstitial lung disease refers to a broad group of inflammatory lung disorders (ILD)
  - AKA pneumoconiosis, diffuse interstitial lung disease, fibrotic interstitial lung disease, pulmonary fibrosis
- Includes more than 180 disease entities characterized by acute, sub-acute, or chronic inflammatory infiltration of alveolar walls by cells, fluid, and connective tissue

Pneumoconiosis

- If left untreated, the inflammatory process can progress to irreversible pulmonary fibrosis
- The ILD group comprises a wide-range of illnesses with varied causes, treatments, and prognoses
- ILDs all reflect similar anatomic alterations of the lungs and cardiopulmonary clinical manifestations

Pneumoconiosis

- Normally pneumoconiosis is a restrictive disease
- Obstruction can occur with accumulation of dust and
- Particulate matter in small airways which may produce:
  - Chronic inflammation
  - Swelling
  - Bronchial obstruction

Anatomic Alterations of the Lungs

- Destruction of alveoli and adjacent pulmonary capillaries
- Fibrotic thickening of resp. bronchioles, alveolar ducts, and alveoli
- Granulomas
- Honeycombing and cavity formation
- Fibrocalcific pleural plaques (asbestosis)

Anatomic Alterations of the Lungs

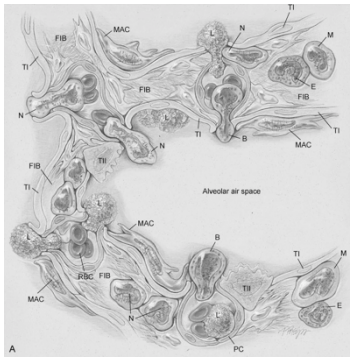
- Bronchospasm
- Airway obstruction caused by inflammation and bronchial constriction
- Bronchial carcinoma
- Mesothelioma (asbestosis)

Anatomic Alterations of the Lungs

- Normally pneumoconiosis is a *restrictive* disease
- *Obstruction* can occur with accumulation of dust and particulate matter in small airways which may produce:
  - Chronic inflammation
  - Swelling
  - Bronchial obstruction

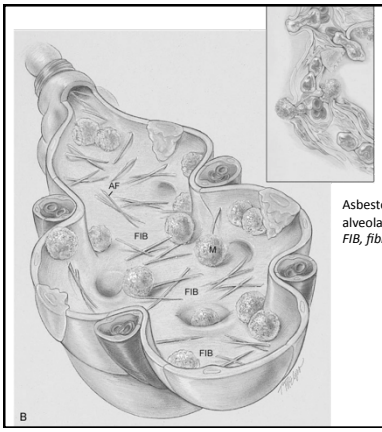
Anatomic Alterations of the Lungs

- Severity depends on
  - The size of the inhaled particles (0.3 - 0.5 μm
  - Chemical nature of inhaled particle
  - Concentration
  - Length of exposure
  - Individual susceptibility

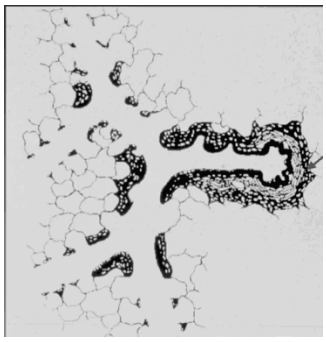


Interstitial lung disease. Cross-sectional microscopic view of alveolar-capillary unit.

B, Basophil; E, eosinophil; FIB, fibroblast (fibrosis); L, lymphocyte; M, monocyte; MAC, macrophage; N, neutrophil; PC, pulmonary capillary; RBC, red blood cell; TI, type I alveolar cell; TII, type II alveolar cell



Asbestosis (close-up of one alveolar unit). *AF, Asbestos fiber; FIB, fibrosis; M, macrophage.*



Dust deposition

Etiology

Occupational, Environmental and Therapeutic Exposures

Inorganic Particulate (dust) Exposure

Asbestos

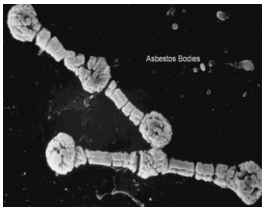
- Asbestosis
  - A common form of ILD
  - Asbestos fibers are a mixture of fibrous minerals composed of hydrous silicates of magnesium, sodium, and iron in various proportions
  - There are two primary types
    - Amphiboles (crocidolite, amosite, and anthophyllite)
    - Chrysotile (most commonly used in industry)
  - Asbestos fibers typically range from 50 to 100 µm in length and are about 0.5 µm in diameter
    - The chrysotiles have the longest and strongest fibers.

Asbestos

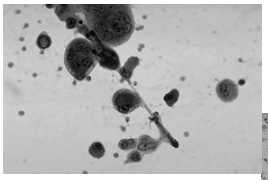
Common Sources of Asbestos Fibers	
Acoustic products	Firefighting suits
Automobile undercoating	Fireproof paints
Brake lining	Insulation
Cements	Roofing materials
Clutch casings	Ropes
Floor tiles	Steam pipe material

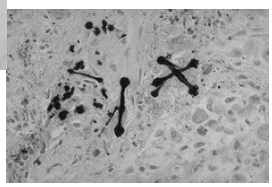
Asbestos

- Asbestos fibers can be seen by microscope within the thickened septa as brown or orange baton-like structures
  - The fibers characteristically stain for iron with Perls' stain
- The pathologic process may affect only one lung, a lobe, or a segment of a lobe
  - The lower lobes are most commonly affected
- Pleural calcification is common and diagnostic in patients with an asbestos exposure history



Asbestos





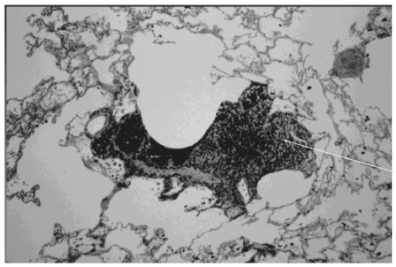
Coal Dust

- Coal Worker's Pneumoconiosis (CWP)
  - The pulmonary deposition and accumulation of large amounts of coal dust
  - Also known as coal miner's lung and black lung
  - Miners who use cutting machines at the coal face have the greatest exposure, but even relatively minor exposures may result in the disease
  - Indeed, cases have been reported in which coal miners' wives developed the disease, presumably from shaking the dust from their husbands' work clothes

Coal Dust

- Simple CWP
  - Characterized by the presence of pinpoint nodules called coal macules (black spots) throughout the lungs
  - The coal macules often develop around the first- and second-generation respiratory bronchioles and cause the adjacent alveoli to retract
- This condition is called focal emphysema

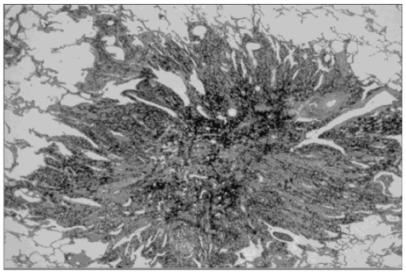
Coal Dust



Coal Dust

- Complicated CWP or progressive massive fibrosis (PMF)
  - Characterized by areas of fibrotic nodules greater than 1 cm in diameter
  - Nodules generally appear in the peripheral regions of upper lobes and extend toward the hilum with growth
    - Composed of dense collagenous tissue with black pigmentation
- Coal dust by itself is chemically inert
  - The fibrotic changes in CWP are usually caused by silica

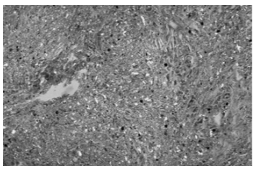
Coal Dust



Silica

- Silicosis (grinder's disease or quartz silicosis)
  - Caused by the chronic inhalation of crystalline, free silica, or silicon dioxide particles
  - Silica is the main component of more than 95% of the rocks of the earth
  - It is found in sandstone, quartz (beach sand is mostly quartz), flint, granite, many hard rocks, and some clays

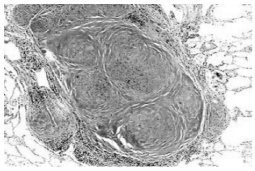
Silica



- Simple silicosis
  - Characterized by small rounded nodules scattered throughout the lungs
  - No single nodule is greater than 9 mm in diameter
  - Patients with simple silicosis are usually symptom-free

Silica

- Complicated silicosis
  - Characterized by nodules that coalesce and form large masses of fibrous tissue, usually in the upper lobes and perihilar regions
  - In severe cases the fibrotic regions may undergo tissue necrosis and cavitate



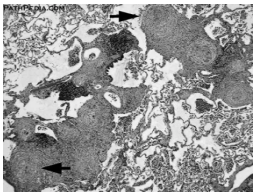
Silica

Common Occupations Associated with Silica Exposure	
Tunneling	Abrasives work
Hard-rock mining	Brick making
Sandblasting	Paint making
Quarrying	Polishing
Stonecutting	Stone drilling
Foundry work	Well drilling
Ceramics work	

Beryllium

- Beryllium
  - Asteel-gray, lightweight metal found in certain plastics and ceramics, rocket fuels, and x-ray tubes
  - Not hazardous as raw ore
  - Processed into the pure metal or one of its salts, however, it may cause a tissue reaction when inhaled or implanted into the skin

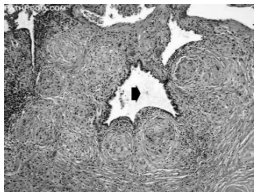
Beryllium



- The acute inhalation of beryllium fumes or particles may cause a toxic or allergic pneumonitis
  - Sometimes accompanied by rhinitis, pharyngitis, and tracheobronchitis

Beryllium

- The more complex form of berylliosis
  - Characterized by the development of granulomas and a diffuse interstitial inflammatory reaction



Additional Inorganic Causes of Interstitial Lung Disease

- Aluminum
  - Ammunition workers
- Baritosis (barium)
  - Barite millers and miners
  - Ceramics workers
- Kaolinosis (clay)
  - Brick makers and potters
  - Ceramics workers
- Siderosis (iron)
  - Welders
- Talcosis (certain talcs)
  - Ceramics workers
  - Papermakers
  - Plastics and rubber workers

Etiology

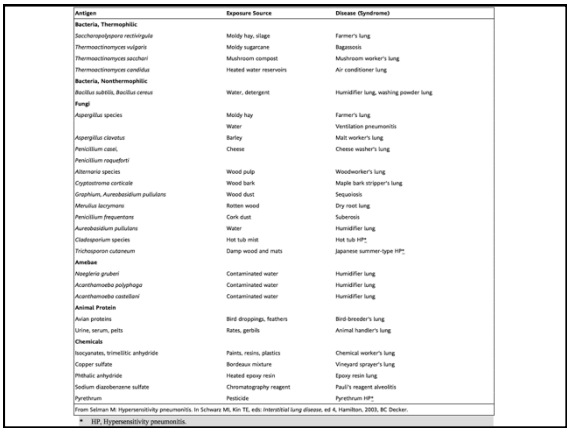
Organic Materials Exposure

Organic Materials Exposure

- Hypersensitivity pneumonitis
  - Also called allergic alveolitis or extrinsic allergic alveolitis) is a cell-mediated immune response of the lungs caused by the inhalation of a variety of offending agents or antigens
  - Such antigens include grains, silage, bird droppings or feathers, wood dust (especially redwood and maple), cork dust, animal pelts, coffee beans, fish meal, mushroom compost, and molds that grow on sugar cane, barley, and straw.

Organic Materials Exposure

- Hypersensitivity pneumonitis
  - The immune response to these allergens causes production of antibody and an inflammatory response
  - The lung inflammation, or pneumonitis, develops after repeated and prolonged exposure to the allergen
    - The term hypersensitivity pneumonitis (or allergic alveolitis) is often renamed according to the type of exposure that caused the lung disorder
    - For example, the hypersensitivity pneumonitis caused by the inhalation of moldy hay is called farmer's lung



Antigen	Exposure Source	Disease (Syndrome)
Bacteria, Thermophilic		
Saccharopolyspora rectivirgula	Moldy hay, silage	Farmer's lung
Thermoactinomyces vulgaris	Moldy sugarcane	Bagassosis
Thermoactinomyces sacchari	Mushroom compost	Mushroom worker's lung
Thermoactinomyces candidus	Heated water reservoirs	Air conditioner lung
Bacteria, Nonthermophilic		
Bacillus subtilis, Bacillus cereus	Water, detergent	Humidifier lung, washing powder lung
Fungi		
Aspergillus species	Moldy hay	Farmer's lung
	Water	Ventilation pneumonitis
Aspergillus clavatus	Barley	Malt worker's lung
Penicillium casei,	Cheese	Cheese washer's lung
Penicillium roqueforti		
Alternaria species	Wood pulp	Woodworker's lung
Cryptostroma corticale	Wood bark	Maple bark stripper's lung
Graphium, Aureobasidium pullulans	Wood dust	Sequoiosis
Merulius lacrymans	Rotten wood	Dry rot lung
Penicillium frequentans	Cork dust	Suberosis
Aureobasidium pullulans	Water	Humidifier lung
Cladosporium species	Hot tub mist	Hot tub HP*
Trichosporon cutaneum	Damp wood and nuts	Japanese summer-type HP*
Amebae		
Naegleria gruberi	Contaminated water	Humidifier lung
Acanthamoeba polyphaga	Contaminated water	Humidifier lung
Acanthamoeba castellani	Contaminated water	Humidifier lung
Animal Protein		
Avian proteins	Bird droppings, feathers	Bird-breeder's lung
Urine, serum, pelts	Rates, gerbils	Animal handler's lung
Chemicals		
Isocyanates, trimellitic anhydride	Paints, resins, plastics	Chemical worker's lung
Copper sulfate	Bordeaux mixture	Vineyard sprayer's lung
Phthalic anhydride	Heated epoxy resin	Epoxy resin lung
Sodium diazobenzene sulfate	Chromatography reagent	Paul's reagent alveolitis
Pyrethrum	Pesticide	Pyrethrum HP*

From Selman M. Hypersensitivity pneumonitis. In Schwarz MI, Kin TE, eds: *Interstitial lung disease*, ed 4, Hamilton, 2003, BC Decker.

* HP, Hypersensitivity pneumonitis.

Organic Materials Exposure

- Medications and illicit drugs
  - As the number of medications and illicit drugs continues to grow, so does the list of possible side effects
  - The lungs are major target organs affected by these side effects
  - Impossible to discuss in detail the various lung-related side effects of every drug

Organic Materials Exposure

- Medications and illicit drugs
  - The chemotherapeutic (anticancer agents) are by far the largest group of agents associated with ILD
  - Nitrofurantoin – antibacterial for UTIs
  - Gold and penicillamine – rheumatoid arthritis
  - Excessive long-term administration of oxygen

Organic Materials Exposure

- Medications and illicit drugs
  - As a general rule, the risk of these drugs causing an interstitial lung disorder is directly related to the cumulative dosage
    - Drug-induced interstitial disease may be seen as early as 1 month to as late as several years after exposure to these agents
  - The precise cause of drug-induced ILD is not known
    - Diagnosis is confirmed by an open lung biopsy
    - When interstitial fibrosis is found with no infectious organisms, a drug-induced interstitial process must be suspected

Organic Materials Exposure

- Radiation Therapy
  - Radiation therapy in the management of cancer may cause ILD
  - Radiation-induced lung disease is commonly divided into the following two major phases
    - the acute pneumonitic phase
    - the late fibrotic phase
  - Acute pneumonitis rarely is seen in patients who receive a total radiation dose of less than 3500 rad

Organic Materials Exposure

- Radiation Therapy
  - Doses in excess of 6000 rad over 6 weeks almost always cause ILD in and near the radiated areas
  - The acute pneumonitic phase develops approximately 2 to 3 months after exposure
  - Chronic radiation fibrosis is seen in all patients who develop acute pneumonitis

Organic Materials Exposure

- Radiation Therapy
  - The late phase of fibrosis may develop
    - immediately after the development of acute pneumonitis
    - without an acute pneumonitic period, or
    - after a symptom-free latent period
  - When fibrosis does develop, it generally does so 6 to 12 months after radiation exposure
    - Pleural effusion often is associated with the late fibrotic phase.

Organic Materials Exposure

- Irritant Gases
  - The inhalation of irritant gases may cause an acute chemical pneumonitis and, in severe cases, ILD
  - Most exposures occur in an industrial setting

Organic Materials Exposure

Gas	Industrial setting
Chlorine	Chemical and plastic industries; water disinfection
Ammonia	Commercial refrigeration; smelting of sulfide ores
Ozone	Welding
Nitrogen dioxide	May be liberated after exposure of nitric acid to air
Phosgene	Used in the production of aniline dyes

Systemic Diseases

- Scleroderma
  - Characterized by chronic hardening and thickening of the skin caused by new collagen formation
    - May occur in a localized form or as a systemic disorder (called systemic sclerosis)
  - Progressive systemic sclerosis (PSS) is a relatively rare autoimmune disorder that affects the blood vessels and connective tissue
    - Causes fibrous degeneration of the connective tissue of the skin, lungs, and internal organs, especially the esophagus, digestive

Systemic Diseases

- Scleroderma
  - Scleroderma of the lung appears as ILD and fibrosis
    - Of all the collagen vascular disorders, scleroderma is the one in which pulmonary involvement is most severe and most likely to cause significant scarring of the lung parenchyma
    - Complications include diffuse interstitial fibrosis, severe pulmonary hypertension, pleural disease, and aspiration pneumonitis
    - May also involve the small pulmonary blood vessels and appears to be independent of the fibrotic process involving the alveolar walls
    - The disease most commonly is seen in women 30 to 50 years of age

Systemic Diseases

- Rheumatoid arthritis
  - primarily an inflammatory joint disease
  - May involve the lungs in the form of
    - Pleurisy, with or without effusion
    - Interstitial pneumonitis
    - Necrobiotic nodules, with or without cavities
    - Caplan's syndrome
    - Pulmonary hypertension secondary to pulmonary vasculitis

Systemic Diseases

- Systemic Lupus Erythematosus
  - Multisystem disorder that mainly involves the joints and skin
  - May cause serious problems in numerous other organs, including the kidneys, lungs, nervous system, and heart
  - Involvement of the lungs appears in about 50% to 70% of the cases

Systemic Diseases

- Systemic Lupus Erythematosus
  - Pulmonary manifestations are characterized by
    - Pleurisy with or without effusion
    - Atelectasis
    - Diffuse infiltrates and pneumonitis
    - Diffuse ILD
    - Uremic pulmonary edema
    - Diaphragmatic dysfunction
    - Infection

Systemic Diseases

- Sarcoidosis
  - Chronic disorder of unknown origin characterized by the formation of tubercles of nonnecrotizing epithelioid tissue
  - Common sites are the lungs, spleen, liver, skin, mucous membranes, and lacrimal and salivary glands, usually with the involvement of the lymph glands

Systemic Diseases

- Sarcoidosis
  - The lung is the most frequently affected organ, with manifestations generally including ILD, enlargement of the mediastinal lymph nodes, or a combination of both
  - One of the clinical hallmarks of sarcoidosis is an increase in all three major immunoglobulins (IgM, IgG, and IgA)

Systemic Diseases

- Sarcoidosis
  - More common among African-Americans and appears most frequently in patients 10 to 40 years of age, with the highest incidence at 20 to 30 years of age
  - Women are affected more often than men, especially among African-Americans

Systemic Diseases

- Idiopathic Interstitial Pneumonia
  - Many patients with ILD do not have a readily identified specific exposure, a systemic disorder, or an underlying genetic cause
  - Such instances of ILD are commonly placed in the idiopathic interstitial pneumonia (IIP) group or the group with specific pathology

Systemic Diseases

- Idiopathic Pulmonary Fibrosis
  - Progressive inflammatory disease with varying degrees of fibrosis and, in severe cases, honeycombing
  - Precise cause is unknown
  - AKA acute interstitial fibrosis of the lung, cryptogenic fibrosing alveolitis, Hamman-Rich syndrome, honeycomb lung, interstitial fibrosis, and interstitial pneumonitis

Systemic Diseases

- Pulmonary Alveolar Proteinosis
  - Condition of unknown cause in which the alveoli become filled with protein and lipids similar pulmonary surfactant
  - Alveolar macrophages generally are dysfunctional in this disorder
  - The disease most commonly is seen in adults 20 to 50 years of age
  - Men are affected twice as often as women

Diffuse Interstitial Lung Diseases

- Goodpasture's Syndrome
  - Disease of unknown cause that involves two organ systems—the lungs and the kidneys
    - In the lungs there are recurrent episodes of pulmonary hemorrhage and in some cases pulmonary fibrosis, presumably as a consequence of the bleeding episodes
    - In the kidneys there is a glomerulonephritis characterized by the infiltration of antibodies within the glomerular basement membrane (GBM)

Diffuse Interstitial Lung Diseases

- Goodpasture's Syndrome
  - Usually is seen in young adults
  - Average survival period after diagnosis is about 15 weeks
  - About 50% of the patients die from massive pulmonary hemorrhage, and about 50% die from chronic renal failure

Overview of the Cardiopulmonary Clinical Manifestations Associated with Interstitial Lung Diseases

The following clinical manifestations result from the pathophysiologic mechanisms caused (or activated) by

- Increased Alveolar-Capillary Membrane Thickness
- Excessive Bronchial Secretions

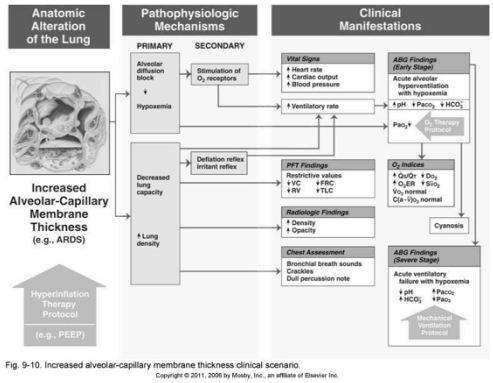


Fig. 9-10. Increased alveolar-capillary membrane thickness clinical scenario.

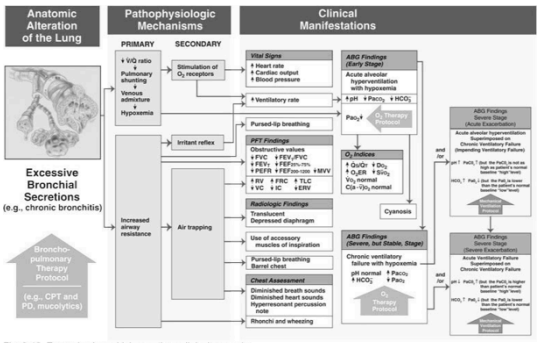


Fig. 9-12. Excessive bronchial secretions clinical scenario.

Clinical Data Obtained at the Patient's Bedside

The Physical Examination

- Vital Signs
  - Increased
    - Respiratory rate (tachypnea)
    - Heart rate (pulse)
    - Blood pressure

The Physical Examination

- Cyanosis
- Digital clubbing
- Peripheral edema and venous distension
  - Distended neck veins
  - Pitting edema
  - Enlarged and tender liver

The Physical Examination

- Nonproductive cough
- Chest Assessment Findings
  - Increased tactile and vocal fremitus
  - Dull percussion note
  - Bronchial breath sounds
  - Crackles, rhonchi
  - Pleural friction rub
  - Whispered pectoriloquy

Clinical Data Obtained from Laboratory Tests and Special Procedures

Pulmonary Function Test Findings

Moderate to Severe ILD
(Restrictive Lung Pathophysiology)

Forced Expiratory Flow Rate Findings

FVC	FEV_T	FEV_1/FVC ratio	$FEF_{25\%-75\%}$
↓	N or ↓	N or ↑	N or ↓

$FEF_{50\%}$	$FEF_{200-1200}$	PEFR	MVV
N or ↓	N or ↓	N or ↓	N or ↓

Pulmonary Function Test Findings

Moderate to Severe ILD
(Restrictive Lung Pathophysiology)

Lung Volume & Capacity Findings

VT	IRV	ERV	RV	VC
N or ↓	↓	↓	↓	↓

IC	FRC	TLC	RV/TLC ratio
↓	↓	↓	N

Decreased Diffusion Capacity

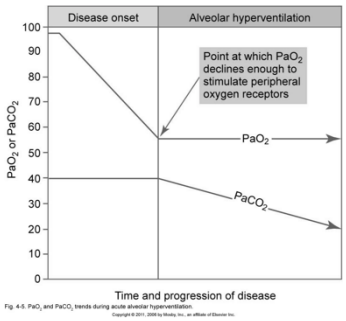
- There is an exception to the expected decreased diffusion capacity in the following two interstitial lung diseases:
  - Goodpasture's syndrome
  - Idiopathic pulmonary hemosiderosis
- The DL_{CO} is often elevated in response to the increased amount of blood retained in the alveolar spaces that is associated with these two disorders.

Arterial Blood Gases

Mild to Moderate ILD

Acute Alveolar Hyperventilation with Hypoxemia
(Interpretation?)

pH	$PaCO_2$	HCO_3	PaO_2
↑	↓	↓ (slightly)	↓



PaO_2 and $PaCO_2$ trends during acute alveolar hyperventilation.

Arterial Blood Gases
Severe chronic ILD

Chronic Ventilatory Failure with Hypoxemia
(Interpretation?)

pH	$PaCO_2$	HCO_3	PaO_2
N	↑	↑ (Significantly)	↓

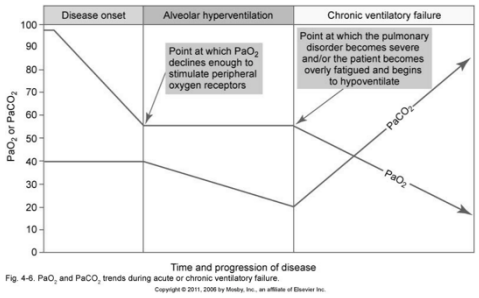


Fig. 4-6. PaO_2 and $PaCO_2$ trends during acute or chronic ventilatory failure.

PaO_2 and $PaCO_2$ trends during acute or chronic ventilatory failure.

Arterial Blood Gases

Acute Ventilatory Changes Superimposed On Chronic Ventilatory Failure

- Because acute ventilatory changes are frequently seen in patients with chronic ventilatory failure, the respiratory care practitioner must be familiar with and alert for the following:
  - Acute alveolar hyperventilation superimposed on chronic ventilatory failure
  - Acute ventilatory failure (acute hypoventilation) superimposed on chronic ventialtory failure

Oxygenation Indices
Moderate to Severe Stage ILD

Q_S/Q_T	DO_2	VO_2	$C(a\text{-}v)O_2$	O_2ER	SvO_2
↑	↓	N	N	↑	↓

Hemodynamic Indices
Severe ILD

CVP	RAP	PA	PCWP	CO	SV
↑	↑	↑	N	N	N

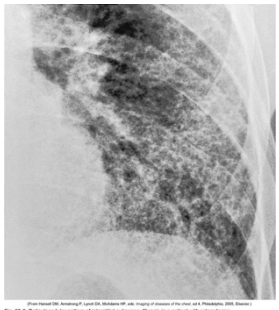
SVI	CI	RVSWI	LVSWI	PVR	SVR
N	N	↑	N	↑	N

Abnormal Laboratory Tests and Procedures

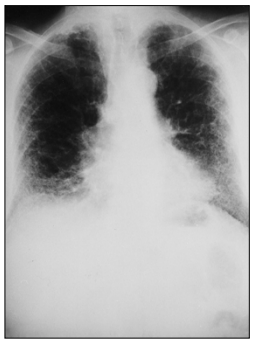
- Hematology
  - Increased hematocrit and hemoglobin (polycythemia)

Radiologic Findings

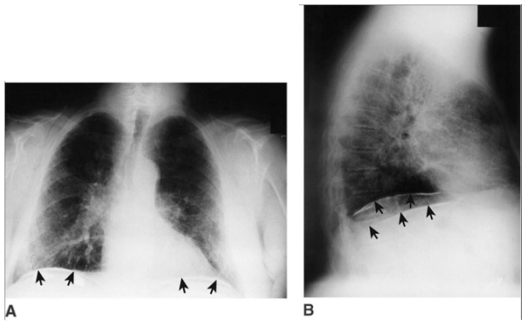
- Chest Radiograph
  - Bilateral reticulonodular pattern
  - Irregularly shaped opacities
  - Granulomas
  - Cavity formation
  - Honeycombing
  - Pleural effusion



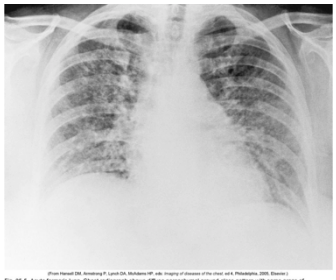
Reticulonodular pattern of interstitial pulmonary fibrosis in a patient with scleroderma.



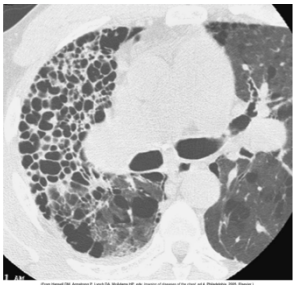
Chest x-ray film of a patient with asbestosis.



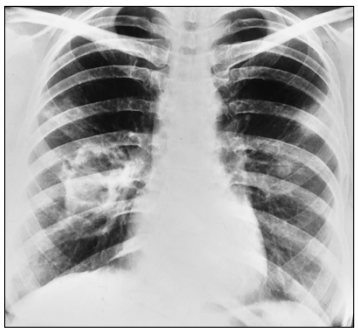
Calcified pleural plaques on the superior border of the diaphragm (*arrows*) in a patient with asbestosis. Thickening of the pleural margins also is seen along the lower lateral borders of the chest. A, Anteroposterior view. B, Lateral view.



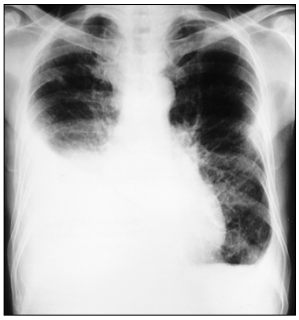
Acute farmer's lung. Chest radiograph shows diffuse parenchymal ground-glass pattern with some areas of consolidation. The severity of parenchymal opacification in this case is unusual.



Honeycomb cysts in sarcoidosis. HRCT through the right midlung shows profuse clustered honeycomb cysts. The cysts are larger than the typical honeycomb cysts seen in usual interstitial pneumonia. Cysts are much less extensive in the left lung.



Wegener's granulomatosis. Numerous nodules with a large (6-cm) cavitary lesion adjacent to the right hilus. Its walls are thick and irregular.



Pleural effusion in rheumatoid disease. Bilateral pleural effusions are present with mild changes of fibrosing alveolitis. The effusions were painless, and the one on the right had been present, more or less unchanged, for 5 months. Note the bilateral "meniscus signs."

General Management of ILD

- Oxygen Therapy Protocol
- Bronchopulmonary Hygiene Therapy Protocol
- Mechanical Ventilation Protocol

General Management of ILD

- Plasmapheresis
  - Treatment of Goodpasture's syndrome is directed at reducing the circulating anti-GBM antibodies that attack the patient's glomerular basement membrane
  - Plasmapheresis, which directly removes the anti-GBM antibodies from the circulation, has been of some benefit