

*Pulmonary Diseases: Structure-Function  
Correlation II*

Parenchymal, Interstitial (Restrictive)  
and Vascular Diseases

Alain C. Borczuk, M.D.  
Dept of Pathology

*Pulmonary Diseases: Structure-Function  
Correlation II*

- Replacement of air with fluid, inflammatory cells or cellular debris
  - Pulmonary Edema
  - Pneumonia
  - Hemorrhage
  - Diffuse alveolar damage pattern (many causes)

*Pulmonary Diseases: Structure-Function  
Correlation II*

**Goals:**

- To observe the relationship between structural/morphologic manifestation of diseases to measurable functional parameters using prototypical diseases of parenchyma, interstitium and vasculature
- To describe the pathology, Gross and microscopic, of these pulmonary diseases.

*Replacement of air with fluid, inflammatory cells  
or cellular debris*

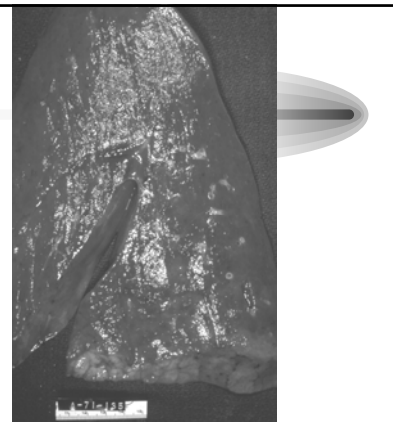
- Pulmonary Edema
  - Generally, increased hydrostatic pressure due to left sided heart disease
  - Gross Pathology - heavy lungs, “wet” with frothy fluid.
  - Microscopic - Edema fluid in alveoli spaces, more severe in lower lobes.

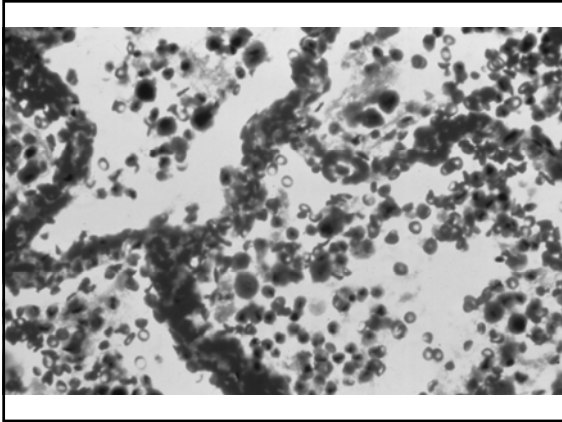
*Pulmonary Diseases: Structure-Function  
Correlation II*

- Disease of the acini and interstitium
  - 1) Replacement of air with fluid, inflammatory cells or cellular debris
  - 2) Thickening of alveolar walls and interstitium
  - 3) Destruction of acinar walls
- Disease of the conducting airways
- Disease of the pulmonary vasculature

Pulmonary  
Edema

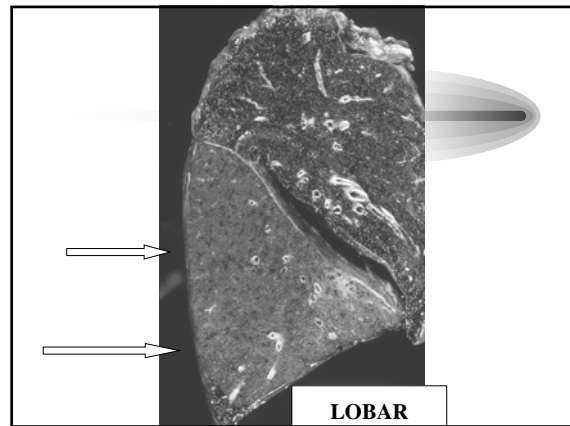
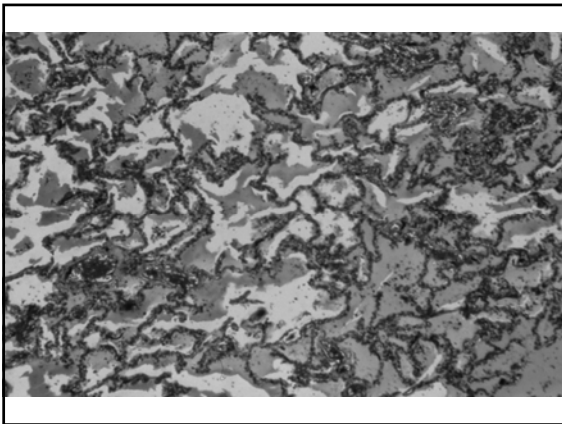
Congested,  
heavy lungs





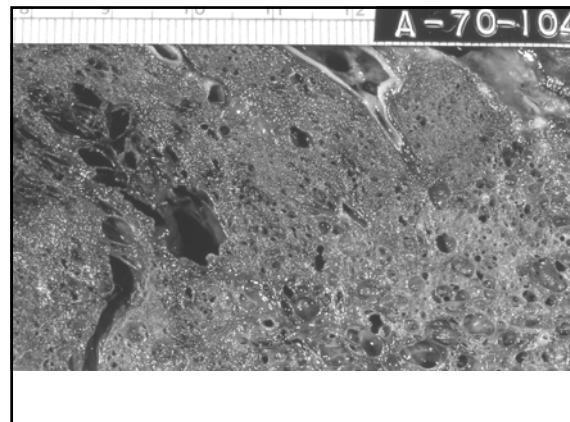
***Replacement of air with fluid, inflammatory cells or cellular debris***

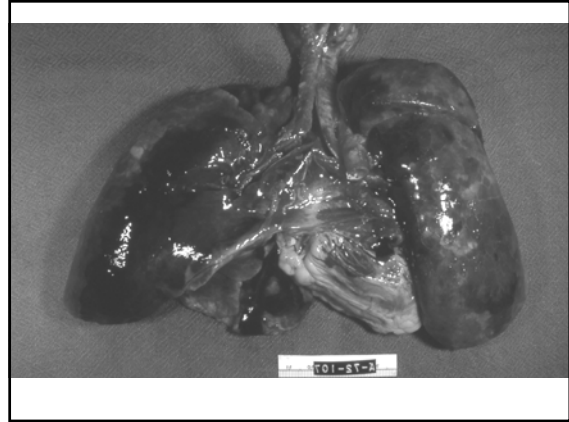
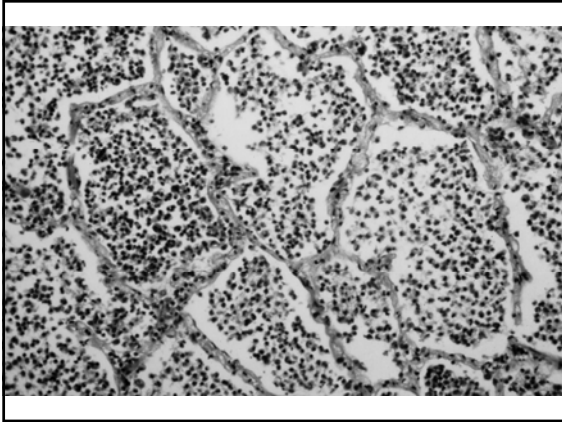
- Pneumonia
  - Inflammation of the lung, often infectious
  - Gross Pathology: Consolidation of lungs (firmness), either small patches or lobar
  - Microscopic: Acute bacterial pneumonia, whether lobar or patchy, is characterized by polymorphonuclear cells filling the alveolar spaces.



***Pulmonary Diseases: Structure-Function Correlation II***

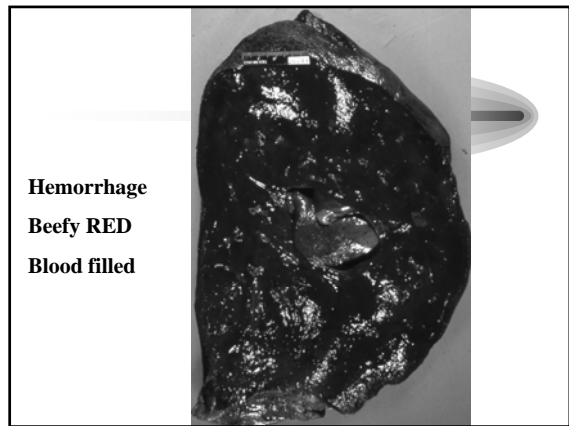
- Replacement of air with fluid, inflammatory cells or cellular debris
  - Pulmonary Edema
  - Pneumonia
  - Hemorrhage
  - Diffuse alveolar damage pattern (many causes)





*Pulmonary Diseases: Structure-Function Correlation II*

- Replacement of air with fluid, inflammatory cells or cellular debris
  - Pulmonary Edema
  - Pneumonia
  - Hemorrhage
  - Diffuse alveolar damage pattern (many causes)



**Hemorrhage**  
**Beefy RED**  
**Blood filled**

*Replacement of air with fluid, inflammatory cells or cellular debris*

- Hemorrhage
  - Filling of alveolar spaces with blood, often with fibrin. If repeated, hemosiderin deposition reflects the chronic component.
  - Causes:
    - Goodpasture's syndrome
    - Pulmonary vasculitis (Wegener's)
    - Structural lesions with vascular erosion, trauma

*Pulmonary Diseases: Structure-Function Correlation II*

- Replacement of air with fluid, inflammatory cells or cellular debris
  - Pulmonary Edema
  - Pneumonia
  - Hemorrhage
  - Diffuse alveolar damage pattern (many causes)

***Replacement of air with fluid, inflammatory cells or cellular debris***

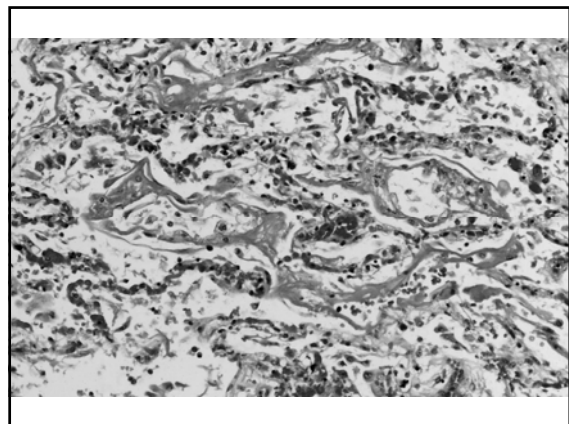
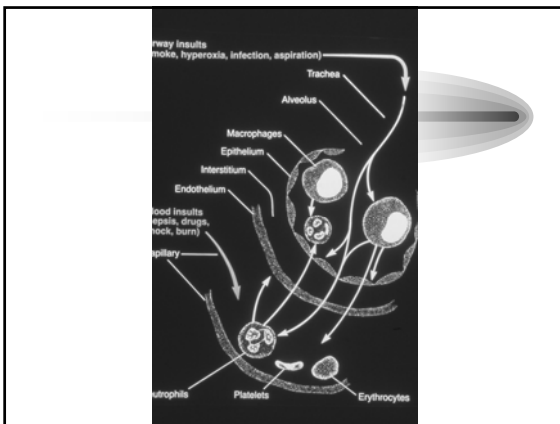
- Diffuse alveolar damage
  - Histology of Adult respiratory distress syndrome (ARDS)
  - Many causes include pulmonary infection, shock, sepsis, pancreatitis, burns, toxic inhalations, radiation, near-drowning
  - Acute alveolar injury with microvascular damage leading to edema and tissue injury.

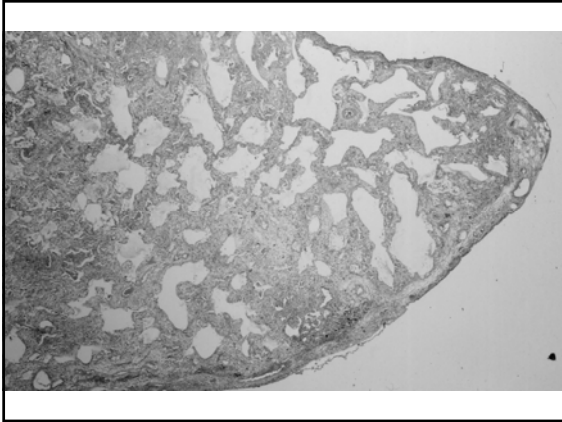
***Replacement of air with fluid, inflammatory cells or cellular debris***

- Diffuse alveolar damage
  - Gross pathology - firm, airless, heavy and “beefy”
  - Microscopic - Stages
    - Earliest - edema followed by hyaline membranes - mixtures of cell debris and fibrin (peaks at 2-3 days)
    - Followed by type II pneumocyte hyperplasia (regeneration)
    - Organization - interstitium with fibroblastic proliferation

***Replacement of air with fluid, inflammatory cells or cellular debris***

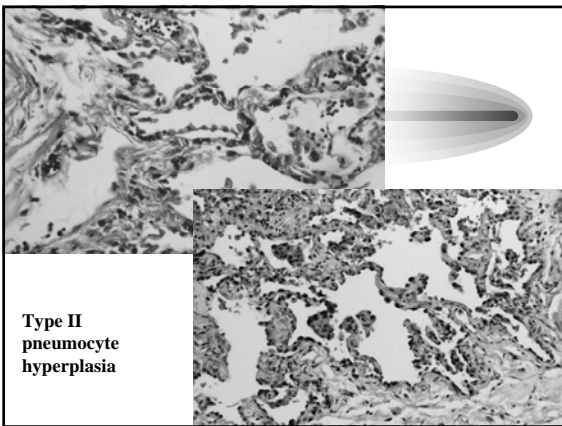
- Diffuse alveolar damage
  - Adult Respiratory Distress Syndrome
    - Acute onset of shortness of breath
    - Hypoxemia
    - Bilateral infiltrates on x-ray
    - Non-cardiogenic
    - .





**Replacement of air with fluid, inflammatory cells or cellular debris**

- Diffuse alveolar damage
  - Bridges diseases of alveolar filling and thickening of interstitium (next section)
  - After the exudative phase, interstitial changes can either resolve or lead to fibrosis (interstitial fibrosis)
  - This acute lung injury is associated with high mortality, especially in the elderly and when associated with sepsis



**Pulmonary Diseases: Structure-Function Correlation II**

- Disease of the acini and interstitium
  - 1) Replacement of air with fluid, inflammatory cells or cellular debris
  - 2) Thickening of alveolar walls and interstitium
  - 3) Destruction of acinar walls
- Disease of the conducting airways
- Disease of the pulmonary vasculature

**Replacement of air with fluid, inflammatory cells or cellular debris**

- | STRUCTURAL  | VS. | FUNCTIONAL  |
|---|-----|---|
| <ul style="list-style-type: none"> <li>• Alveoli filled with blood, neutrophils, hyaline membranes, or fluid</li> </ul> |     | <ul style="list-style-type: none"> <li>• Decreased lung volume (atelectasis)</li> <li>• Increase in shunt flow</li> <li>• In DAD, edema, hypoxic vasoconstriction and vascular injury may cause pulmonary hypertension</li> </ul> |

**Pulmonary Diseases: Structure-Function Correlation II**

- Thickening of alveolar walls and interstitium
  - Idiopathic pulmonary fibrosis/usual interstitial pneumonia
  - Sarcoidosis
  - Hypersensitivity pneumonitis

*Pulmonary Diseases: Structure-Function Correlation II*

- Thickening of alveolar walls and interstitium
  - Restrictive lung diseases
  - Interstitium can be thickened by inflammatory cells – lymphocytes, histiocytes, granulomas, or fibrosis/fibroblastic proliferation or a combination of both

*Pulmonary Diseases: Structure-Function Correlation II*

- Thickening of alveolar walls and interstitium
  - Idiopathic pulmonary fibrosis/usual interstitial pneumonia
  - Sarcoidosis
  - Hypersensitivity pneumonitis

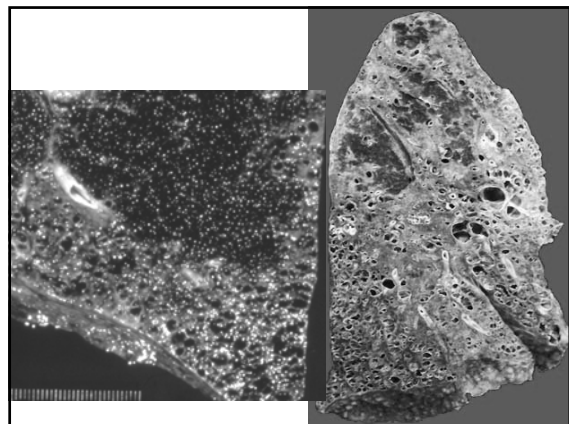
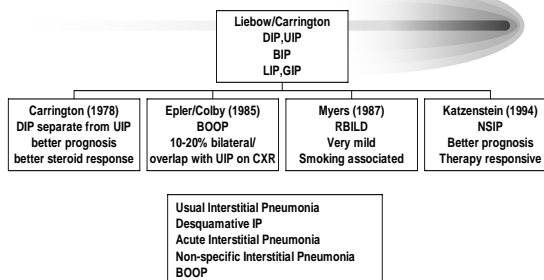
*Thickening of alveolar walls and interstitium*

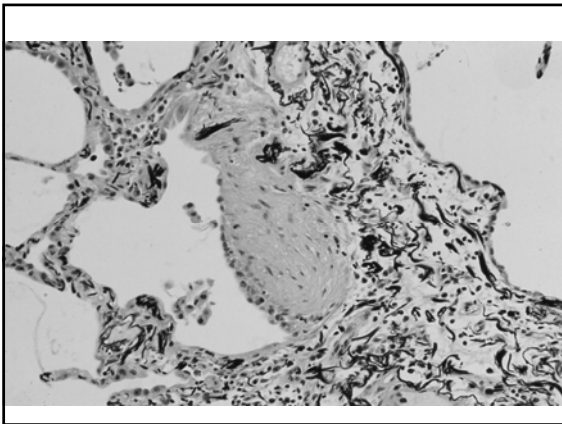
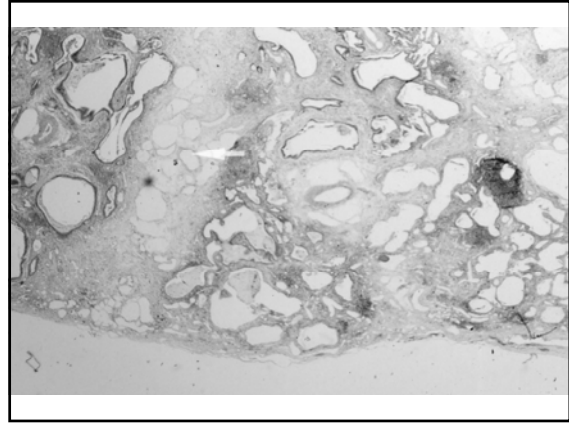
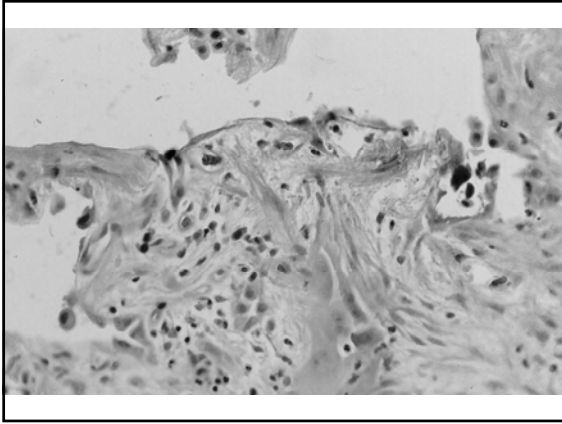
- Injuries can be associated with diffuse or patchy involvement, and can have varying degrees of cellularity. Cellularity has some prediction of treatment response, although underlying cause/disease is also important.
- Inflammatory processes are usually steroid responsive
- Dense fibrosis is irreversible

*Thickening of alveolar walls and interstitium*

- Usual interstitial pneumonia
  - Idiopathic pulmonary process characterized by progressive pulmonary fibrosis
  - Small foci of lung injury lead to fibroblastic proliferation and fibrosis
  - New foci appear alongside normal lung and densely fibrotic lung
  - Mortality is high and disease is resistant to therapy

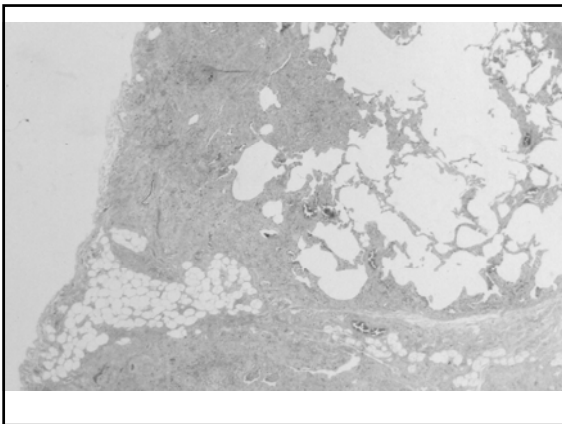
*Historical evolution*



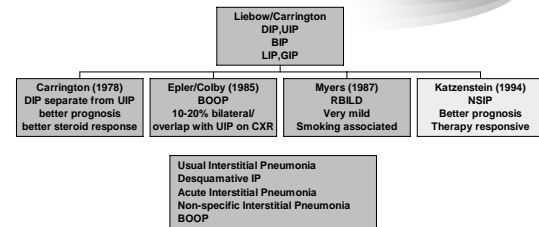


*Thickening of alveolar walls and interstitium*

- | STRUCTURAL   | VS. | FUNCTIONAL   |
|--|-----|--|
| <ul style="list-style-type: none"> <li>• Usual interstitial pneumonia                             <ul style="list-style-type: none"> <li>- Gross Pathology - Fibrosis involving subpleural areas, leading to "honeycomb" pattern</li> <li>- Microscopic - peripheral lobular fibrosis, dense, with small foci of fibroblastic proliferation; sparing of airways</li> </ul> </li> </ul> |     | <ul style="list-style-type: none"> <li>• Lung compliance decreased</li> <li>• Lung volume decreased</li> <li>• Lung recoil increased; airways remain open</li> <li>• V/Q mismatch - ventilation unevenly affected.</li> <li>• Diffusion reduced, defect elicited by exercise.</li> <li>• RESTRICTIVE disease.</li> </ul> |



*Historical evolution*

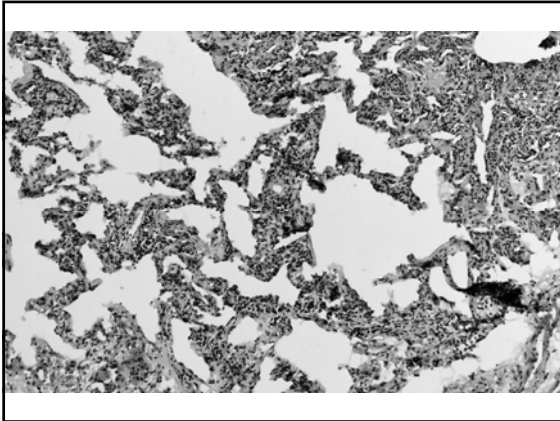


### *Non-specific interstitial pneumonia*

- **Katzenstein and Fiorelli (1994)**
  - Uniform age of injury and diffuse involvement of lobule.
  - Predominance of chronic inflammatory cells.
  - Vary from cellular to fibrotic
  - Average age (44), associated connective tissue disease, dust exposure, EAA
  - Cellular form, 100% alive at 5 years; worsens with increased fibrosis.

### *Pulmonary Diseases: Structure-Function Correlation II*

- Thickening of alveolar walls and interstitium
  - Idiopathic pulmonary fibrosis/usual interstitial pneumonia
  - Sarcoidosis
  - Hypersensitivity pneumonitis

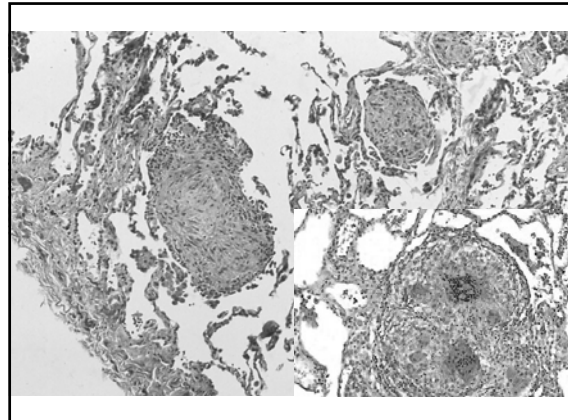


### *Thickening of alveolar walls and interstitium*

- **Sarcoidosis**
  - Idiopathic disease characterized by non-necrotizing granulomas in hilar nodes and pulmonary interstitium
  - Can be systemic, and involve skin, eyes/lacrimal glands, and salivary glands (heart, CNS, pituitary also)
  - Remissions can be spontaneous or induced by steroid therapy
  - Most patients recover; some develop respiratory impairment; some progress to end stage fibrosis (10%)

### *Why do we classify?*

- Some patterns are associated with systemic diseases (e.g. NSIP in collagen vascular disease), or fibrosis due to certain medications
- The idiopathic interstitial pneumonia have different rates of progression to fibrosis
- Steroid responsiveness is high for some diseases (NSIP, BOOP) and low to non-existent for others (UIP)
- Mortality rates, likelihood of progression, decision to treat with cytotoxic agent, and candidacy for transplant may all be affected by the classification



*Pulmonary Diseases: Structure-Function  
Correlation II*

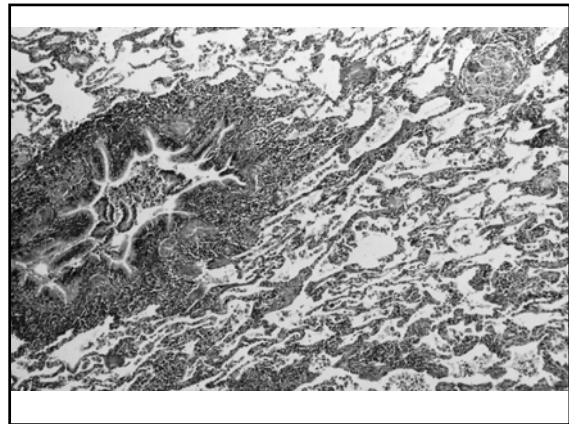
- Thickening of alveolar walls and interstitium
  - Idiopathic pulmonary fibrosis/usual interstitial pneumonia
  - Sarcoidosis
  - Hypersensitivity pneumonitis

*Thickening of alveolar walls and interstitium*

- Hypersensitivity pneumonitis (extrinsic allergic alveolitis)
  - Pathology
    - Expansion of peribronchial lymphoid tissue
    - Mild chronic interstitial pneumonitis
    - Interstitial histiocytic collections

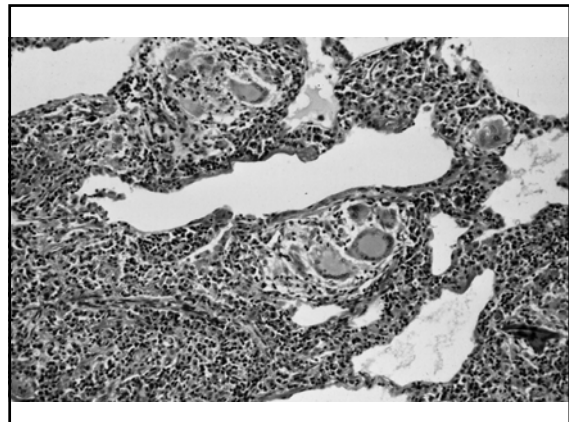
*Thickening of alveolar walls and interstitium*

- Hypersensitivity pneumonitis (extrinsic allergic alveolitis)
  - Immunologically mediated (type III/typeIV) lung disease caused by inhalation of organic antigen. Patients have circulating antibodies, complement activation and granuloma formation
  - Named after circumstances surrounding antigen exposure:
    - Pigeon breeder's lung
    - Farmer's lung - thermophilic actinomycetes
    - Humidifier lung - thermophilic bacteria
    - Duck feather fever - duck feather
    - Maple bark disease
    - Mushroom picker's lung



*Thickening of alveolar walls and interstitium*

- Hypersensitivity pneumonitis (extrinsic allergic alveolitis)
  - Patients experience fever, cough, malaise, dyspnea.
  - Acutely, patients may link an exposure with symptoms, but chronic form can be more insidious and therefore detailed history may be needed to make a connection
  - Steroid responsive, but can lead to fibrosis in some patients with untreated chronic antigen exposure



### *Thickening of alveolar walls and interstitium*

#### **In summary:**

There are a group of restrictive lung diseases characterized by increase in inflammatory cells or fibroblasts in the interstitium/alveolar walls. While they can all lead to fibrosis, some diseases do so invariably (UIP) and others less commonly (NSIP, sarcoid, hypersensitivity). In addition, diseases which are characterized by inflammation are usually steroid responsive. UIP does not respond well to any therapy and therefore has a high mortality.

This is why we attempt to classify these diseases by their inflammation and their patterns of fibrosis.

### *Pulmonary Diseases: Structure-Function Correlation II*

- Disease of the pulmonary vasculature
  - Pulmonary embolism
  - Pulmonary hypertension

### *Thickening of alveolar walls and interstitium*

Also of note is that fibrosing lung disease can be caused both by idiopathic processes, as well as by certain known processes such as asbestos exposure or collagen vascular disease, for example scleroderma.

Some use the term cryptogenic, because even though we know that immunologic reaction can lead to fibrosis, we do not know why some patients with identical exposure or diseases do not develop lung disease

### *Pulmonary Diseases: Structure-Function Correlation II*

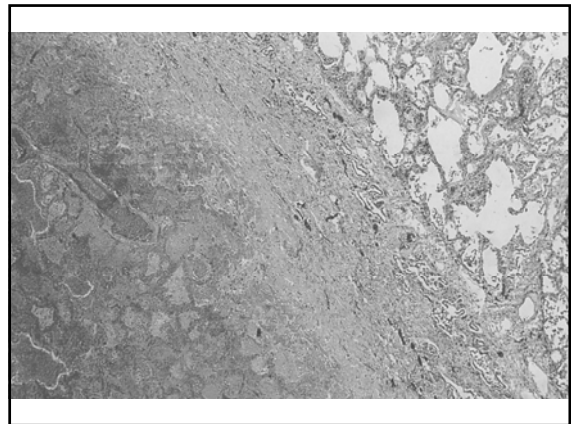
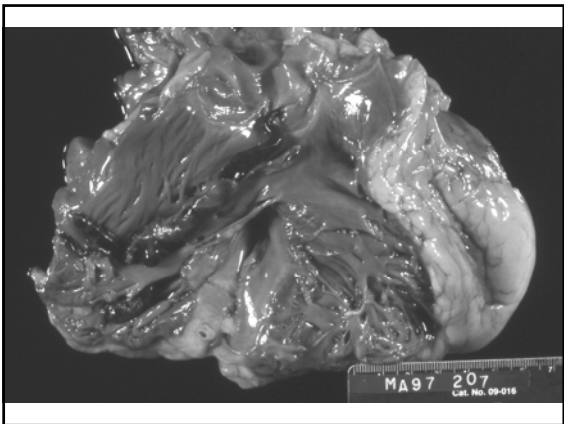
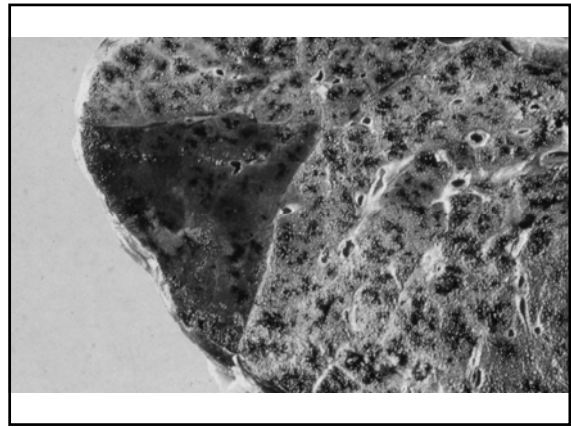
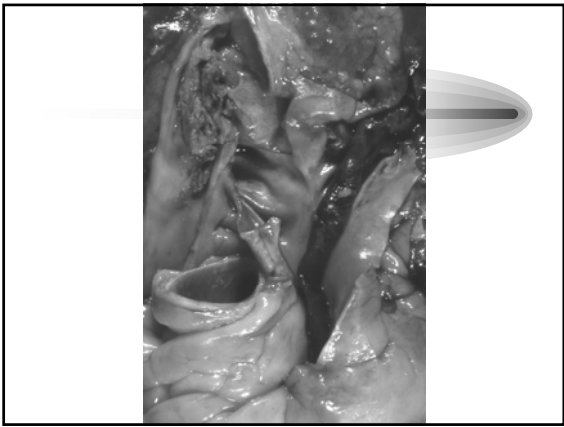
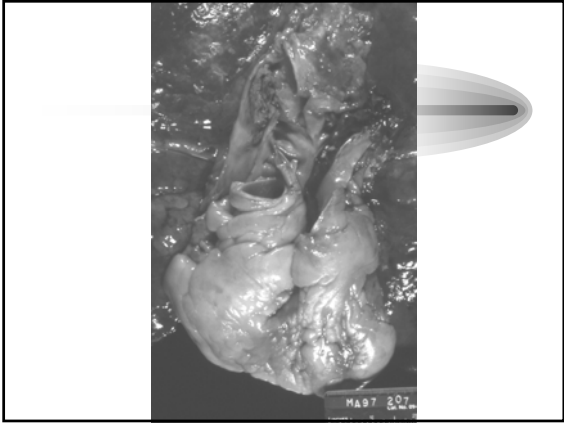
- Disease of the pulmonary vasculature
  - Pulmonary embolism
  - Pulmonary hypertension

### *Pulmonary Diseases: Structure-Function Correlation II*

- Disease of the acini and interstitium
  - 1) Replacement of air with fluid, inflammatory cells or cellular debris
  - 2) Thickening of alveolar walls and interstitium
  - 3) Destruction of acinar walls
- Disease of the conducting airways
- Disease of the pulmonary vasculature

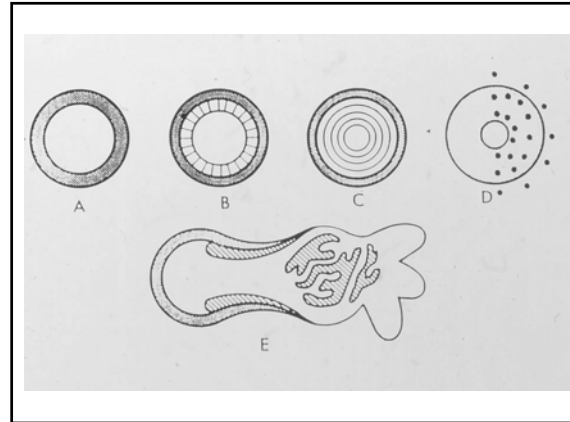
### *Disease of the pulmonary vasculature*

- Pulmonary embolism
  - Pathology
    - The majority of PE arise from deep venous thrombosis of the lower extremity.
    - Can occlude pulmonary artery at bifurcation (saddle embolus) or pulmonary artery branches
    - Results in infarct only 10% of the time, and infarctions are hemorrhagic when they occur
    - Small emboli organize and recanalize. Chronic PE can lead to pulmonary hypertension



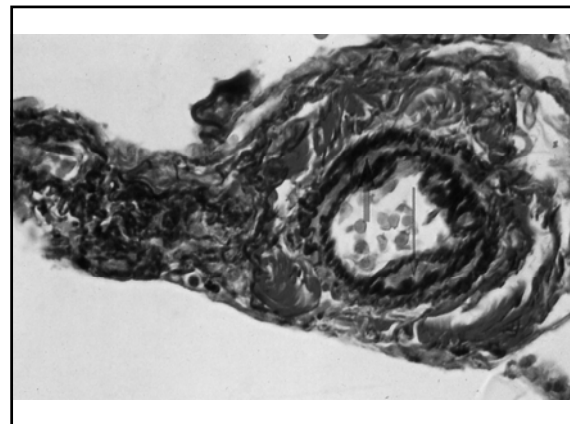
*Pulmonary Diseases: Structure-Function  
Correlation II*

- Disease of the pulmonary vasculature
  - Pulmonary embolism
  - Pulmonary hypertension



*Disease of the pulmonary vasculature*

- Pulmonary hypertension
  - Gross pathology
    - Pulmonary artery atherosclerosis and dilatation
    - Right ventricular hypertrophy and dilatation, depending on time course of the disease
  - Microscopic pathology
    - Progressive abnormalities reflect severity and duration of hypertension



*Disease of the pulmonary vasculature*

- Pulmonary hypertension
  - Grading System - Heath and Edwards
    - Grade 1 - hypertrophy of medial smooth muscle
    - Grade 2 - Intimal proliferation
    - Grade 3 - Intimal proliferation with fibrosis and luminal narrowing
    - Grade 4,5 - Complex lesions, with network of capillary like channels, angiomatous and cavernous lesions
    - Grade 6 - Necrosis of vessel wall

