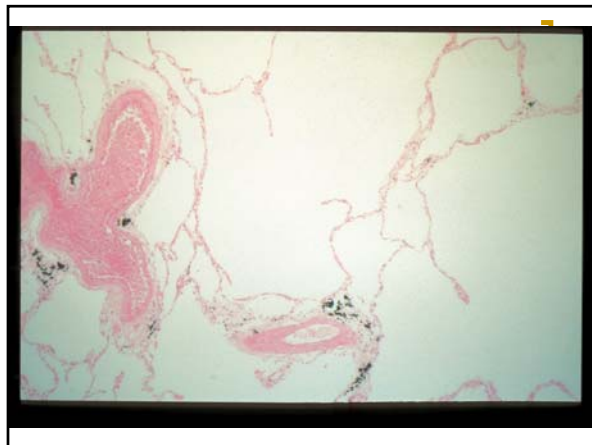
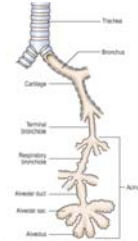


## Interstitial Lung Disease

## Pulmonary interstitium

- Alveolar lining cells (types 1 and 2)
- Thin elastin-rich connective component containing capillary blood vessels



## Interstitial lung disease

- Increase in interstitial tissue causing “stiffness”
- Physiological restrictive defect
- Alveolar-capillary interface is site of injury
- Acute and chronic disease
- Lots of causes/patterns!

## Interstitial lung disease

- Early stage and acute is *alveolitis* (injury with inflammatory cell infiltration)
- Late stage characterised by *fibrosis*

Clinical effects due to hypoxia (respiratory failure) and cardiac failure

## Causes....

- Environmental (mineral dusts, drugs, radiation. Post-ARDS)
    - Hypersensitivity (mouldy hay, avian proteins)
  - Unknown (idiopathic)
    - Connective tissue diseases
    - Idiopathic pulmonary fibrosis
- Diagnosis based on clinical features often with biopsy

### Biopsy in interstitial lung disease...

- Transbronchial biopsy – special forceps used at bronchoscopy
- Thoracoscopic biopsy – more invasive but more reliable and generates far more tissue

### ARDS (adult respiratory distress syndrome)

- Classic model of acute interstitial injury
- Diffuse alveolar damage syndrome (DADS)
- Shock lung
  - Causes include sepsis, diffuse infection (virus, mycoplasma), severe trauma, oxygen

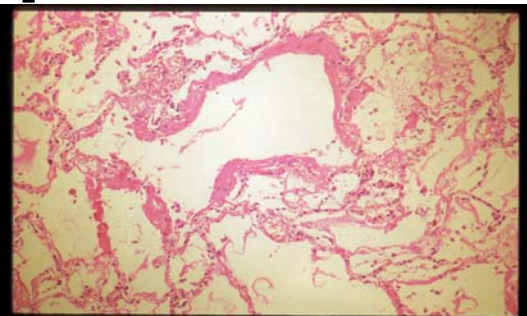
### Pathogenesis of ARDS

- Injury (eg bacterial endotoxin)
- Injury to cell membranes (*either alveolar epithelial cells or endothelial cells*)
  - Infiltration of inflammatory cells
  - Cytokines
  - Oxygen free radicals

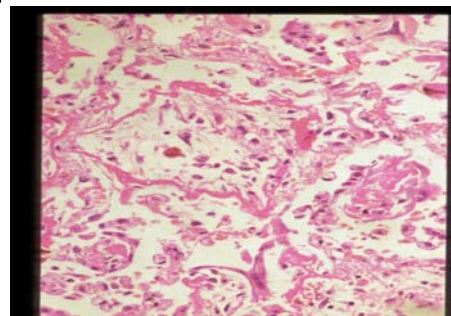
### Pathology of ARDS

- Fibrinous exudate lining alveolar walls (hyaline membranes)
- Cellular regeneration
- Inflammation

### ARDS with hyaline membrane



### ARDS – cellular reaction

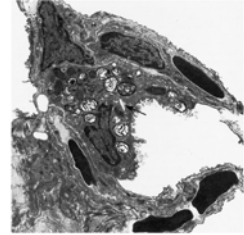


## Outcome of ARDS

- Death
- Resolution
- Fibrosis (chronic restrictive lung disease)

## Neonatal RDS

- Premature infants
- Deficient in surfactant (type 2 alveolar lining cells)
- Increased effort in expanding lung physical damage to cells



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## Chronic Interstitial Disease

- Idiopathic pulmonary fibrosis (IPF)
- Sarcoidosis
- Extrinsic allergic alveolitis (hypersensitivity pneumonitis)
- Pneumoconiosis
- Connective tissue diseases

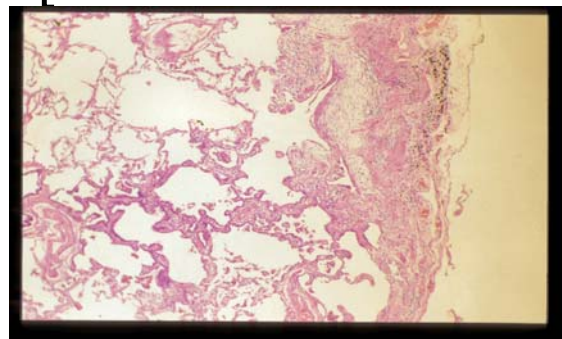
## IPF

- aka cryptogenic fibrosing alveolitis (CFA), usual interstitial pneumonia (UIP)
- Progressive interstitial fibrosis of unknown cause
- Variable associated inflammation
- Finger clubbing

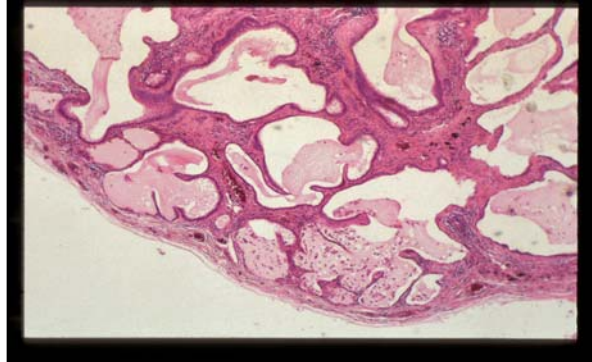
## Pathology

- Subpleural and basal fibrosis
- Inflammatory component variable
- Terminally lung structure replaced by dilated spaces surrounded by fibrous walls

## Fibrosing alveolitis (early)



### [ IPF (late – honeycombing) ]

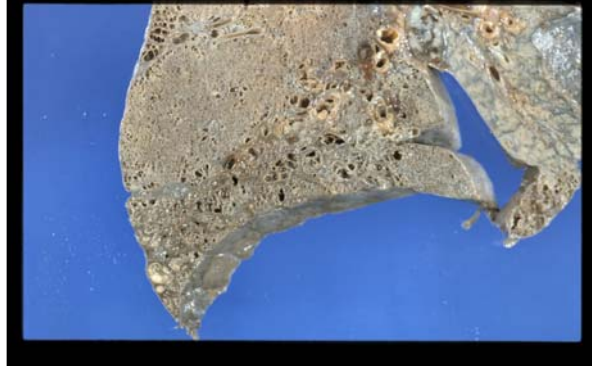


### [ Honeycomb lung ]

- Subpleural “enlarged” spaces with fibrous walls
- A powerful “splint” effect – like a plaster cast



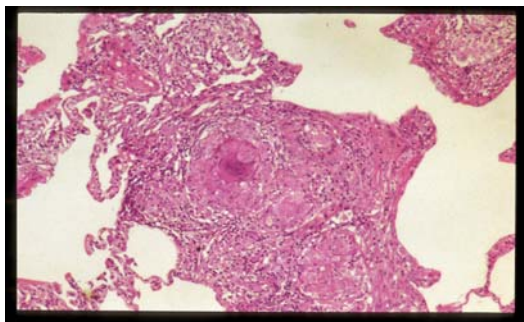
### [ Honeycombing – basal/subpleural (a splint!) ]



### [ Extrinsic allergic alveolitis (hypersensitivity pneumonitis) ]

- Chronic *inflammatory* disease
  - Small airways
  - Interstitium
  - Occasional granulomas
- Allergic origin
  - Type III hypersensitivity
  - Type IV hypersensitivity

### [ Inflammation in hypersensitivity pneumonitis ]



### [ Causes of EAA ]

- Thermophilic bacteria – Farmers lung
- Avian proteins – Bird fanciers lung
- Fungi – Malt workers lung

Precipitins (antibodies) often detectable in serum. Unusual cases come to biopsy.



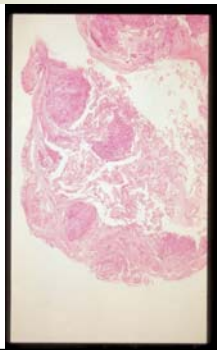
## Sarcoidosis

- Multisystem *granulomatous* disorder of unknown cause (defined by histological means)
- Pulmonary involvement is common
- Most cases mild and self-limiting
- In US 10 times commoner in black vs. white

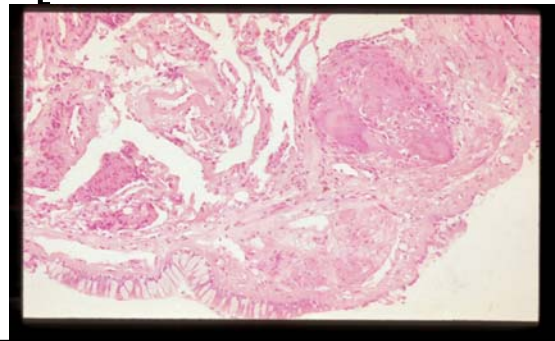
## Other manifestations of sarcoidosis

- Uveitis (inflammation of iris)
- Erythema nodosum
- Lymphadenopathy
- Hypercalcaemia

## Transbronchial biopsy - sarcoidosis



## Sarcoidosis - granuloma



## Pulmonary involvement in connective tissue diseases

- Interstitial fibrosis (milder than fibrosing alveolitis)
- Pleural effusions
- Rheumatoid nodules

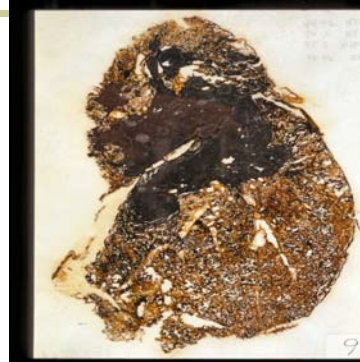
## Pneumoconiosis

- Lung disease caused by mineral dust exposure
- Asbestosis
  - Coal workers lung
  - Silicosis

Thin whole mount section of a coal-workers lung (unstained)



Coal miner with progressive massive fibrosis (unstained)



### Disease depends on....

- Particle size (1-5 $\mu$ m)
- Reactivity of particle
- Clearance of particle
- Host response

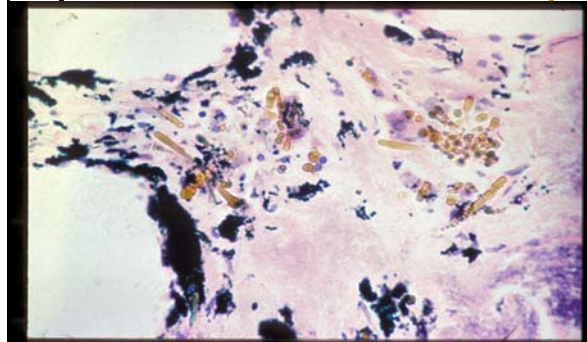
### Asbestos

- A silicate
- Serpentine (curved) asbestos fibres relatively safe
- Straight (amphibole) asbestos highly dangerous

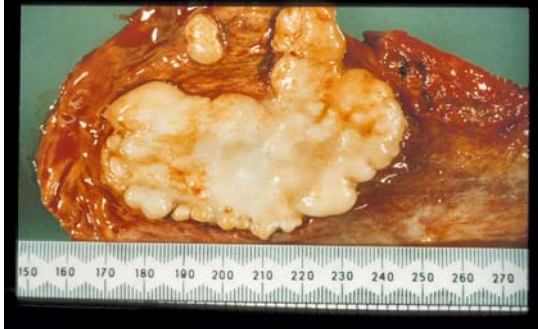
Asbestosis bodies (from human lung)



Association of asbestos bodies with fibrosis (asbestosis)



Pleural plaque on diaphragm



## Pulmonary eosinophilia

- Alveolar infiltration by eosinophils:
- Tropical eosinophilia – associated with migration of microfilariae through the lung
  - Other eosinophilic “pneumonias” – a range of immune responses
  - Often acutely sensitive to treatment with steroids