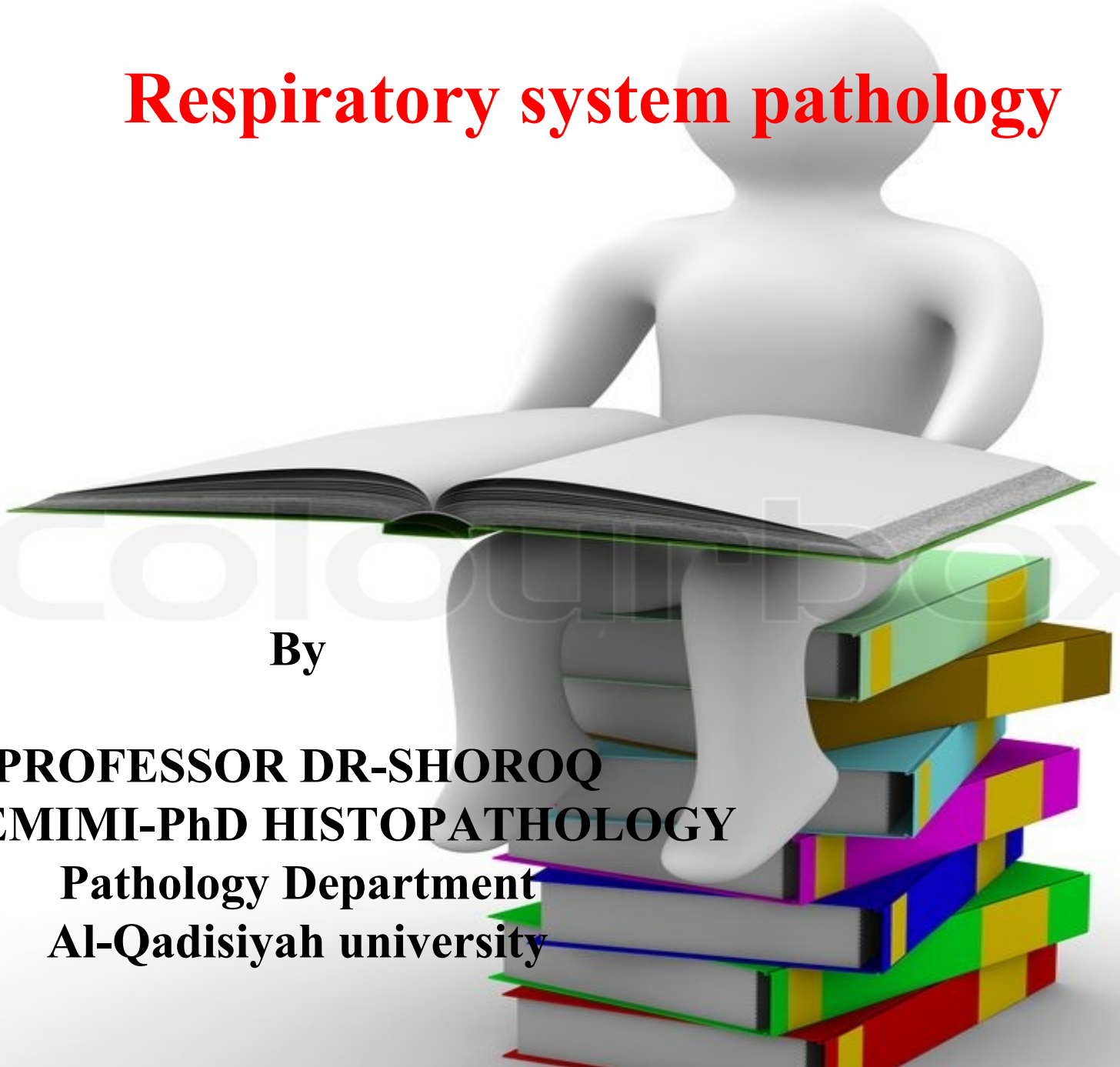
Respiratory system pathology



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Learning objectives

1- Chronic Diffuse Interstitial (Restrictive) Diseases

A-Definition (can not get air in)

B-Pathogenesis

C-Microscopical features

2-Pulmonary hypertension

A-Definition

B-Pathogenesis

C-Microscopical features

Chronic Diffuse Interstitial (Restrictive) Diseases

-Chronic interstitial diseases are a heterogeneous group of disorders characterized predominantly by an inflammatory process involving the alveolar wall (resulting in widespread fibroelastic proliferation and collagen deposition) that can lead to irreversible fibrosis, distortion of lung architecture, and impaired gas exchange.

-Many of the entities are of unknown cause and pathogenesis, some have an intra-alveolar as well as an interstitial component.

These disorders account for about 15% of noninfectious diseases seen by pulmonary physicians.

Pathogenesis

Restrictive Lung Diseases

Parenchymal

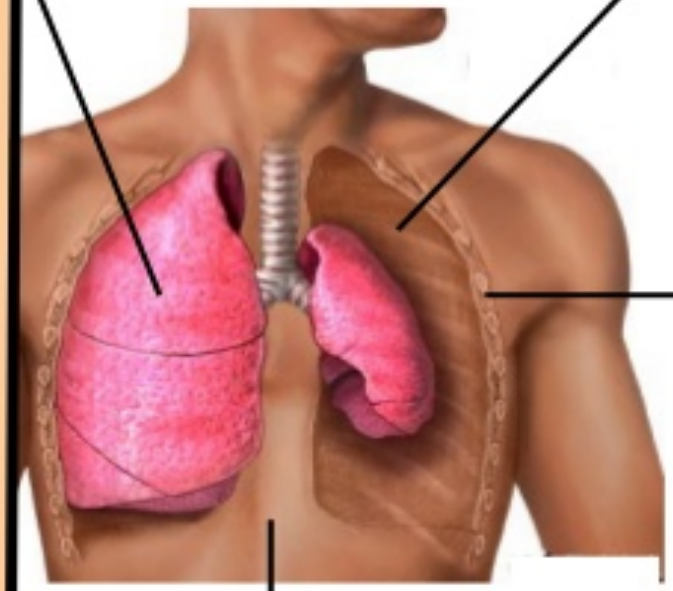
-Extra Parenchymal

Lung

Interstitial Pulmonary Fibrosis (IPF):

- 1ry (Idiopathic)
- Occupational
- Collagenic
- Granulomatous
- Irradiation
- Resection
- Drug induced

(Bleomycin, Methotrexate, Cyclophosphamide)



Pleura

- Pleural effusion
- Pneumothorax
- Pleural fibrosis
- Pleural tumours
- Pleural thickening

Chest Wall

- Trauma
- Kyphoscoliosis
- Ankylosing Spondylitis
- Neuromuscular Disease (Myasthenia/Guillain Barre)
- Morbid obesity
- Scleroderma

Abdomen

Severe Distension

Idiopathic pulmonary fibrosis

A. Fibrosis of lung interstitium
B. Etiology is unknown. Likely related to cyclical lung injury; TGF-p from injured pneumocytes induces fibrosis.

Occupational pulmonary fibrosis (Pneumoconiosis)

The pneumoconiosis are a group of interstitial lung diseases caused by the inhalation of certain dusts and the lung tissue's reaction to the dust. The principal cause of the pneumoconioses is work-place exposure; environmental exposures have rarely given rise to these diseases. Alveolar macrophages engulf foreign particles and induce fibrosis.

Summary of Pneumoconioses

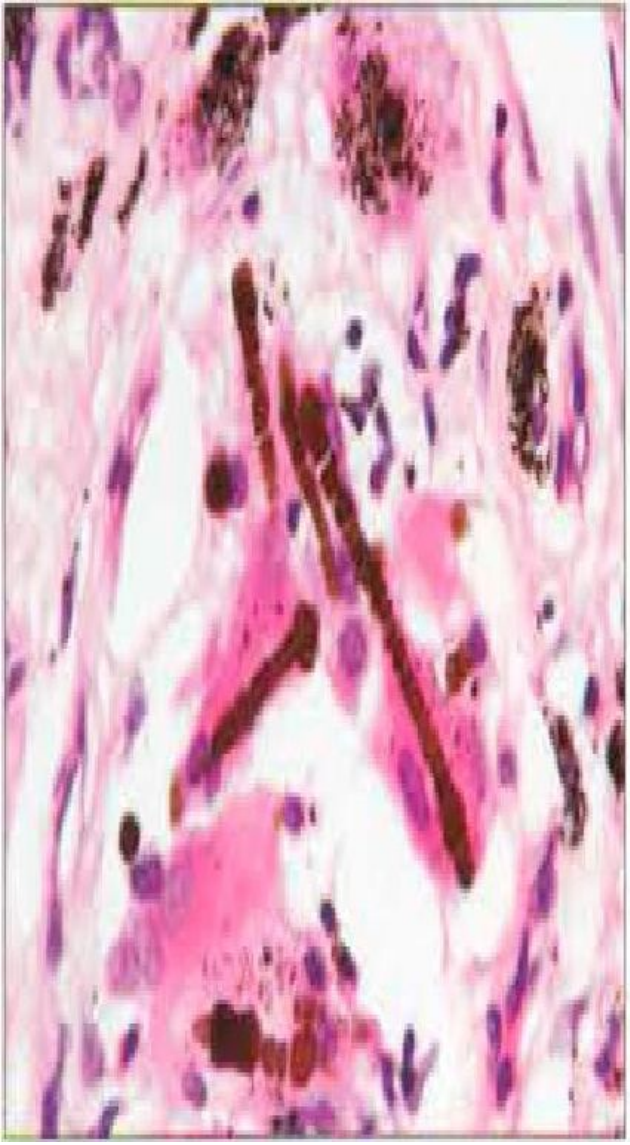
ENTITY	EXPOSURE	PATHOLOGIC FINDINGS	COMMENTS
Coal Workers' Pneumoconiosis	Carbon dust; seen in coal miners	Massive exposure leads to diffuse fibrosis ('black lung'); associated with rheumatoid arthritis (Caplan syndrome)	Mild exposure to carbon (e.g., pollution) results in anthracosis (collections of carbon-laden macrophages); not clinically signid cant
Silicosis	Silica; seen in sand blasters and silica miners	Fibrotic nodules in upper lobes of the lung	Increased risk for TB; silica impairs phagolysosome formation by macrophages.
Berylliosis	Beryllium; seen in beryllium miners and workers in the aerospace industry	Noncaseating granulomas in the lung, hilar lymph nodes, and systemic organs	Increased risk for lung cancer
Asbestosis	Asbestos fibers; seen in construction workers, plumbers, and shipyard workers	Fibrosis of lung and pleura [plaques) with increased risk for lung carcinoma and mesothelioma; lung carcinoma is more common Ihan mesothelioma in exposed individuals.	Lesions may contain long, golden-brown fibers with associated iron (asbestos bodies, Fig, 9.14), which confirm exposure to asbestos

Sarcoidosis

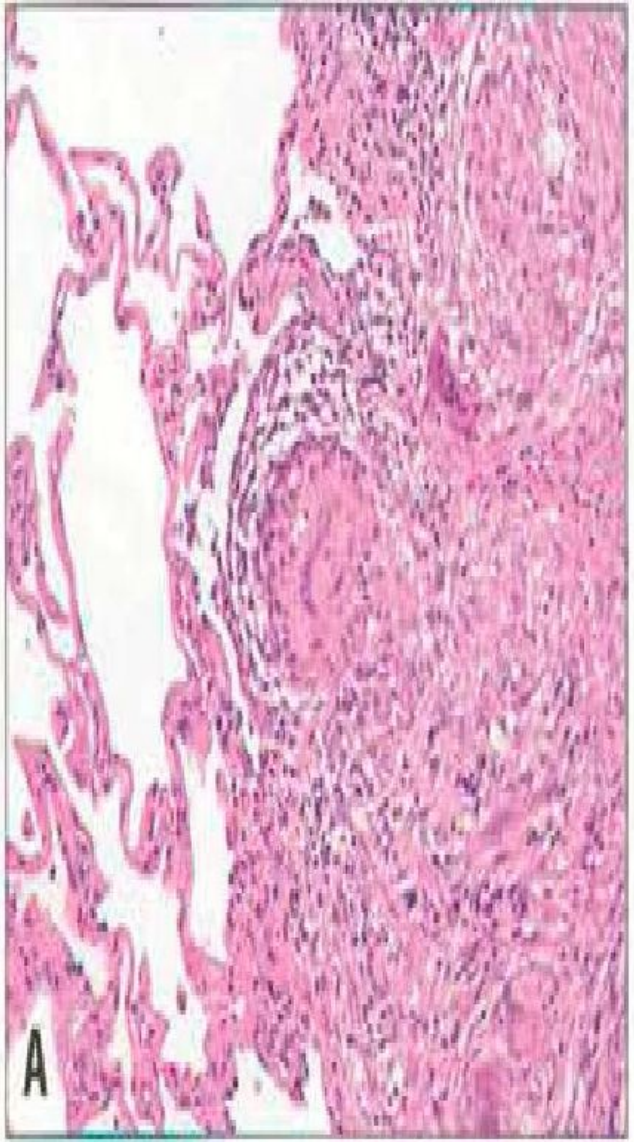
A. Systemic disease characterized by non caseating granulomas in multiple organs; classically seen in African American females

B. Etiology is unknown; likely due to CD4' helper T-cell response to an unknown antigen

C. Granulomas most commonly involve the hilar lymph nodes and lung ,leading to restrictive lung disease. Characteristic stellate inclusions 'asteroid bodies' are often seen within giant cells of the granulomas

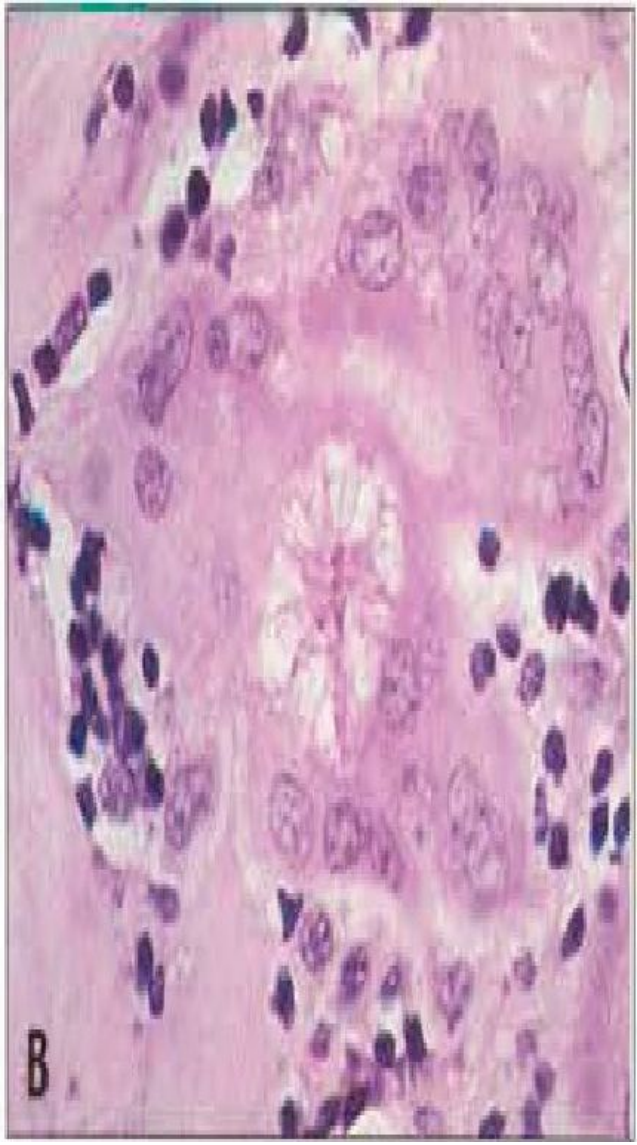


Asbestos bodies



Sarcoidosis.

A. Non caseating granuloma involving lung



B- Asteroid body

Hypersensitivity pneumonitis

A. Granulomatous reaction to inhaled organic antigens (e.g., pigeon breeder's lung)

B. Presents with fever, cough, and dyspnea hours after exposure; resolves with removal of the exposure.

C. Chronic exposure leads to interstitial fibrosis

-Secondary causes of interstitial fibrosis such as drugs (e.g., bleomycin (chemotherapy for bladder cancer)and amiodarone(antihypertensive drug) and radiation therapy must be excluded.

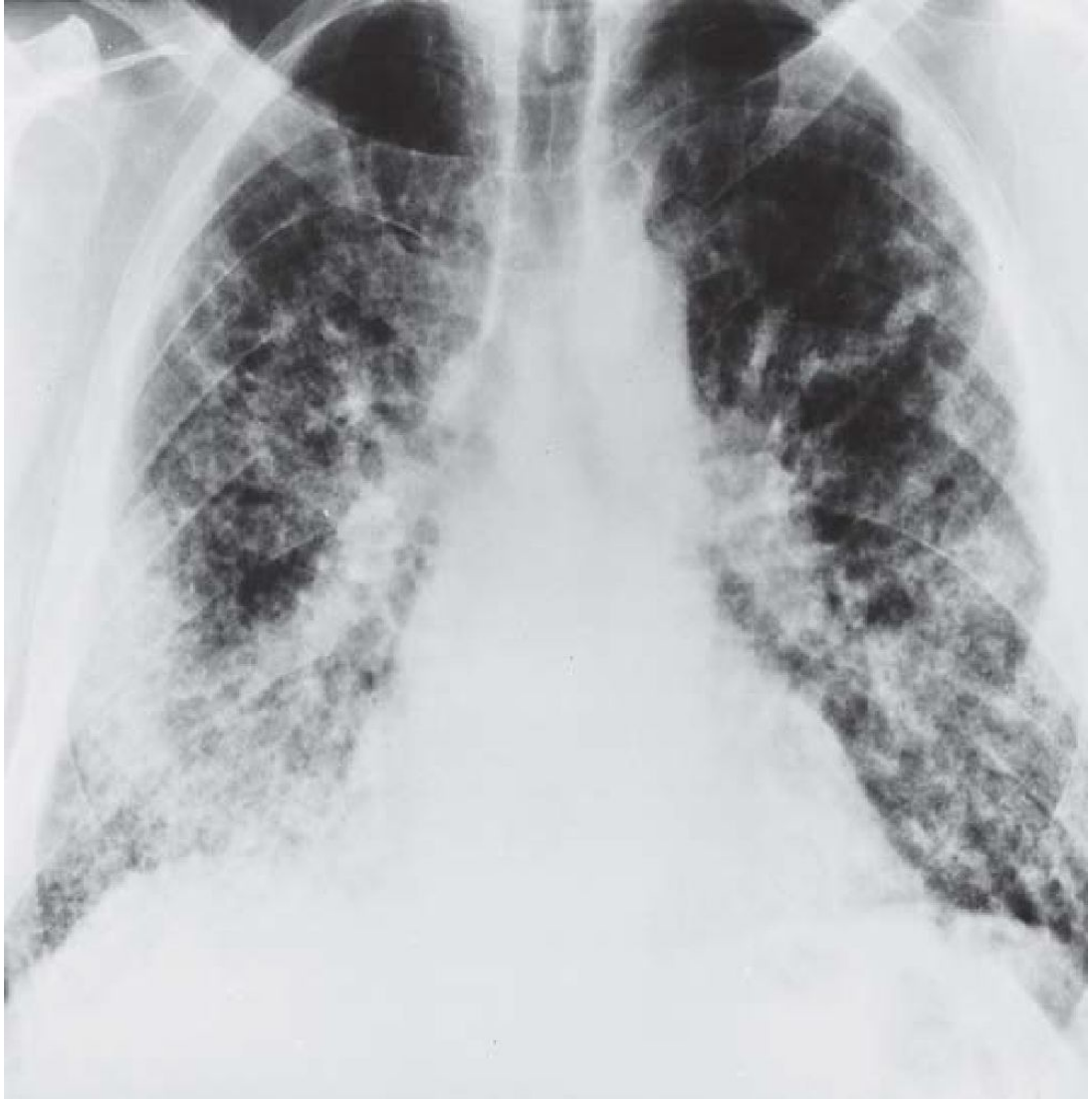
Clinical features

1- Dyspnea (at first with exertion; later at rest)
2- Cough (non productive)
3- Fatigue
4-Without wheezing or other evidence of airway obstruction.
5-Reductions in lung volume(collapse)
6-Chest radiographs show bilateral infiltrative lesions in the form of small nodules, irregular lines, or ground-glass shadows.

Later on lead to :-

7-Secondary pulmonary hypertension and right-sided heart failure with cor- pulmonale may result.

Although the entities can often be distinguished in the early stages, the advanced forms are hard to differentiate because they result in scarring and gross destruction of the lung, often referred to as end-stage lung or honeycomb lung.



CXR ;- shows extensive pulmonary fibrosis.

DIFFERENT BETWEEN OBSTRUCTIVE VS. RESTRICTIVE

Obstructive disorders	Restrictive disorder
• Decrease in both FEV1 and FEV1/FVC ratio .	• Normal FEV1/FVC ratio .

Forced vital capacity (FVC):
The maximum volume of air forcibly exhaling from the point of maximal inhalation.

Forced expiratory volume in 1 second (FEV1):
Forced expiratory volume in 1 second during FVC maneuver.

Ratio of FEV1 and FVC (FEV1/FVC):
Expressed as percentage

Take home message

-There are many causes of chronic interstitial lung disease.

-Diffuse interstitial fibrosis of the lung gives rise to restrictive lung diseases characterized by reduced lung compliance and reduced forced vital capacity (FVC). The ratio of FEV1 to FVC is normal or near normal.

-It may result in respiratory failure or cor pulmonale

Pulmonary hypertension

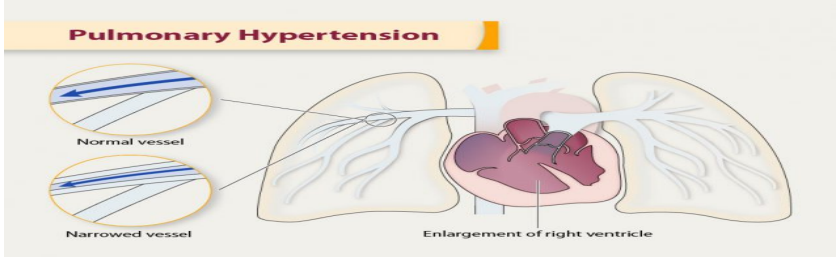
Pulmonary hypertension is a type of high blood pressure that affects the arteries in the lungs and the right side of the heart. In which blood vessels in the lungs are narrowed, blocked or destroyed.

A. high pressure in the pulmonary circuit (mean arterial pressure > 25 mm Hg of systemic level at rest ; normal is 10 mm Hg).

B. Leads to right ventricular hypertrophy with eventual cor pulmonale

C. Presents with exertional dyspnea or right-sided heart failure .

Pathogenesis of PHT



pulmonary endothelial cell and/or vascular smooth muscle dysfunction is the probable underlying basis for most forms of pulmonary hypertension.

PHT was sub classified as primary or secondary based on etiology.

Primary pulmonary hypertension

A. Classically seen in young adult females(20-40 y)

B, Etiology is unknown; some familial forms are related to inactivating mutations of bone morphogenetic protein receptor 2 (BMPR2) signaling pathway..

In vascular smooth muscle cells (SMCs), BMPR2 signaling inhibits proliferation and favors apoptosis; defective signaling therefore results in SMC hyperplasia (leading to proliferation of vascular smooth muscle) and increased vascular resistance

Secondary pulmonary hypertension

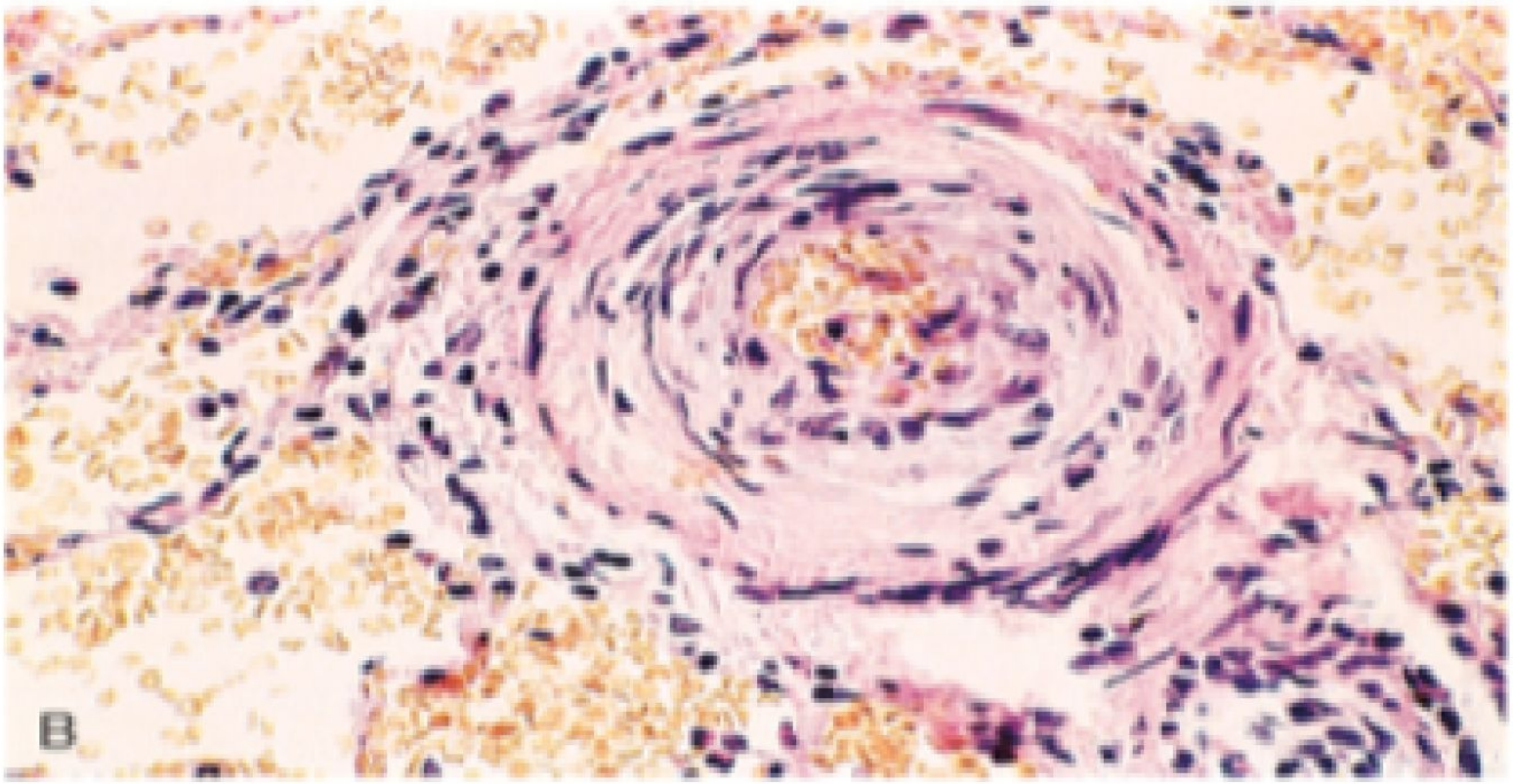
In states of secondary pulmonary hypertension, endothelial cell dysfunction arises as a consequence of the underlying disorder

1-Mechanical injury due to increased blood flow in left-to-right shunts and increased volume in the pulmonary circuit (e.g., congenital heart disease).

2- Biochemical injury produced by fibrin in recurrent thromboembolism), and hypoxemia (e.g., COPD and interstitial lung disease) which are induce endothelial cell dysfunction reduces production of vasodilatory agents (e.g., nitric oxide, prostacyclin) . while increasing synthesis of vasoconstrictive mediators like endothelin. In addition, there is production of growth factors and cytokines that induce the migration and replication of vascular smooth muscle and elaboration of extracellular matrix.

Microscopical features of PHT

Characterized by atherosclerosis of the pulmonary trunk (in majority of cases) , smooth muscle hypertrophy of pulmonary arteries, and intimal fibrosis; are seen with severe, long-standing disease .



B, PHT :-Narrowed lumen Marked medial hypertrophy, and intimal fibrosis; are seen with severe, long-standing disease


What we learn with
pleasure
we never forget