FIBROSING DISEASES

Disease	morphology	Clinical features	Notes
Idiopathic pulmonary fibrosis (usual interstitial pneumonia)	-patchy, progressive bilateral interstitial fibrosis. -**Cobblestones appearance** of the pleural surface, due to retraction of scars along the interlobular septa. -The cut surface shows fibrosis (firm, rubbery white areas). -Temporal heterogeneity is typical (early and late lesions coexist): • Fibroblastic foci are fibroblastic proliferations and considered the earliest lesions. • Late lesions are more collagenous and less cellular and may show honeycomb fibrosis.	-Gradual onset of Nonproductive cough and progressive dyspnea. -On physical exam, "dry" or "Velcro"-like crackles during inspiration. -Cyanosis, cor pulmonale, and peripheral edema may develop later. -The overall prognosis remains poor. -survival is only 3 to 5 years. -lung transplantation is the only definitive treatment. -Management: Anti-inflammatory therapies, Anti-fibrotic therapies.	-Males, Never before 50s -Diagnosis of exclusion, radiologic and histologic pattern are needed. -Repeated cycles of epithelial activation/injury by some unidentified agent, Defective repair of alveolar epithelium, Genetic predisposition (telomerase, surfactant, MUC5B variant). -Lower lobe and subpleural regions and along the interlobular septa are mostly affected. -also known as cryptogenic Fibrosing alveolitis.
Nonspecific Interstitial Pneumonia	-patchy but uniform mild to moderate interstitial chronic inflammation and/or fibrosis.	-Dyspnea and cough of several months. -frequent association with collagen vascular disorders such as rheumatoid arthritis. -Better prognosis than IPF.	-Chronic bilateral interstitial lung disease of Unknown etiology. - despite its name it has Distinct clinical, radiologic, and histologic features.
Cryptogenic Organizing Pneumonia	-**chest x-ray:** subpleural or peribronchial patchy airspace consolidation. -**Microscopically**: Intraalveolar plugs of loose organizing connective tissue.	-Cough and dyspnea -Some patients recover spontaneously while most require treatment, usually with oral steroids.	- Uncommon - Unknown etiology

Pneumoconiosis

*lung reaction to inhalation of mineral dusts, organic and inorganic particulates, chemical fume and vapor.
*The most common mineral dust are induced by inhalation of Coal dust, silica, and asbestos.
*usually related to workplace exposure, except for Asbestos.
*The reaction depends on size, shape, solubility, and reactivity of the particles. Particles that are 1 to 5 µm in diameter are the most dangerous.
*The pulmonary alveolar macrophage is a key cellular element of lung injury and fibrosis.
*Tobacco smoking worsens the effects of all inhaled mineral dusts, more so with asbestos .
* PMF is confluent fibrosing reaction in the lung, can be a complication of any one of the pneumoconiosis.
*Refer to the table in slide 26 of lecture 5

Disease	morphology	Clinical features	Notes
Coal Worker's Pneumoconiosis (CWP)	Simple CWP: **• Presence of coal macules and nodules. Coal macules: dust-laden macrophages small amounts of collagen fibers arrayed in a delicate network.** **centrilobular emphysema can occur.** Complicated CWP (PMF): **• coalescence of coal nodules that develops over many years.** **• multiple, dark black scars >2 cm & up to 10 cm consist of dense collagen and pigment.**	1-Asymptomatic anthracosis**: pigment accumulates without a cellular reaction.** 2- Simple coal worker's pneumoconiosis (CWP): **accumulations of macrophages with little to no pulmonary dysfunction.** 3- Complicated CWP or progressive massive fibrosis (PMF)**: extensive fibrosis and compromised lung function. increasing pulmonary dysfunction, pulmonary ht, and cor pulmonale.** **• less than 10% of cases of simple CWP progress to PMF**	**-Coal is mainly carbon, in addition to other inorganic minerals.** **-Pulmonary Anthracosis: Seen also in urban dwellers and tobacco smokers.** **- Inhaled carbon pigment is engulfed by alveolar or interstitial macrophages, accumulate in the connective tissue along the pulmonary and pleural lymphatics and in draining lymph nodes.** **- Upper lobes and upper zones of the lower lobes are more heavily involved.** **- The Progression from CWP to PMF is linked to higher coal dust exposure levels and total dust burden.** **- once established PMF has a tendency to progress even in the absence of further exposure.** **- No increased risk of lung carcinoma in coal miners. Distinguishes CWP from silica and asbestos exposures.**

Silicosis	**Macroscopically:** • early stages are tiny, barely palpable, discrete, pale-to-black (if coal dust is present) nodules. **Microscopically:** • Silicotic nodules: Concentrically arranged hyalinized collagen fibers surrounding amorphous center. With "whorled" collagen fibers. • Polarized microscopy reveals weakly birefringent silica. • Nodules may coalesce into hard, collagenous scars, with eventual progression to PMF. • Fibrotic lesions also may occur in hilar lymph nodes and pleura.	• **Asymptomatic:** detected as fine nodularity in the upper zones of the lung on routine chest radiographs. • **after PMF:** Shortness of breath, pulmonary hypertension and cor pulmonale. - slowly progressive, impairing pulmonary function to a degree that limits physical activity. -Increased susceptibility to tuberculosis (impaired cell mediated immunity). -relationship with lung cancer is controversial.	- The most prevalent chronic occupational disease in the world. -Inhalation of crystalline silica mostly in occupational settings. - Workers in sandblasting and hard-rock mining are at high risk. -quartz is the most common crystalline form implicated in silicosis. -Amorphous silica is less pathogenic. -When mixed with other minerals, the fibrogenic effect of quartz is reduced, this fortuitous situation is commonplace, as quartz in the workplace is rarely pure. -**Upper zones of the lungs** -After inhalation, the particles interact with epithelial cells and macrophages, Activating the inflammasome and the release of inflammatory mediators by pulmonary macrophages (IL-1, TNF, fibronectin, lipid mediators, oxygen-derived free radicals, and fibrogenic cytokines.)
Asbestosis	- diffuse pulmonary interstitial fibrosis (the first to appear), indistinguishable from UIP. -**Asbestos bodies:** golden brown, fusiform or beaded rods with a translucent center. Formed of asbestos fibers coated with an iron-containing proteinaceous material. -**Pleural plaques**: the most common manifestation of asbestos exposure, well-circumscribed plaques of dense	• Progressively worsening dyspnea 10 to 20 years after exposure. • cough and production of sputum. • static or progress to congestive heart failure, cor pulmonale, and death. • Pleural plaques are usually asymptomatic.	**ASSOCIATED WITH:** (1) parenchymal interstitial fibrosis (asbestosis); (2) localized fibrous plaques or, rarely, diffuse pleural fibrosis. (3) pleural effusions (4) Lung carcinomas (5) malignant pleural and peritoneal mesotheliomas (6) laryngeal carcinoma.

	collagen containing calcium, on anterior and posterolateral aspects of the parietal pleura and over the domes of the diaphragm	**OUTCOMES:** • The risk for developing lung carcinoma is increased 5-fold for asbestos workers. • the relative risk for mesothelioma is more than 1000 times greater than the risk for lung cancer. • Concomitant cigarette smoking increases the risk for lung carcinoma but not for mesothelioma. • Lung or pleural cancer associated with asbestos exposure carries a particularly poor prognosis.	-once phagocytosed by macrophages asbestos fibers activate the inflammasome and damage phagolysosomal membranes, release of proinflammatory factors and fibrogenic mediators→ 1. cellular and fibrotic lung reactions 2. tumor initiator and a promoter mediated by the oncogenic effects of reactive free radicals generated by asbestos fibers on the mesothelium. -The adsorption of carcinogens in tobacco smoke onto asbestos fibers results in remarkable synergy between tobacco smoking and the development of lung carcinoma in asbestos workers. - The risk of cancer is increased in family members of asbestos workers and to individuals exposed outside of the workplace. -Begins in the lower lobes and subpleurally.

PULMONARY EOSINOPHILIA

Disease	Morphology	Clinical features	notes
Acute eosinophilic pneumonia with respiratory failure		rapid onset of fever, dyspnea, hypoxia. respond to corticosteroids.	The bronchoalveolar lavage fluid typically contains more than 25% eosinophils

Simple pulmonary eosinophilia (Loeffler syndrome)	the alveolar septa are thickened by an infiltrate containing eosinophils and occasional giant cells	Benign clinical course	• transient pulmonary lesions • eosinophilia in the blood
Tropical eosinophilia*:*			caused by infection with microfilariae and helminthic parasites.
Secondary eosinophilia		association with asthma, drug allergies, and certain forms of vasculitis	
Idiopathic chronic eosinophilic pneumonia*:*	characterized by aggregates of lymphocytes and eosinophils within the septal walls and the alveolar spaces, typically in the periphery of the lung	high fever, night sweats, and dyspnea	disease of exclusion, once other causes of pulmonary eosinophilia have been ruled out.

SMOKING RELATED INTERSTITIAL DISEASES

Disease	Morphology	Clinical features
Desquamative interstitial pneumonia (DIP)	• The most striking histologic feature of DIP is the accumulation of large numbers of macrophages containing dusty-brown pigment *(smoker's macrophages)* in the air spaces. • Alveolar septa are thickened by sparse inflammatory infiltrate (usually lymphocytes). • +/- mild Interstitial fibrosis.	• good prognosis • excellent response to steroids and smoking cessation, however, some patients progress despite therapy.
respiratory bronchiolitis	• presence of pigmented intraluminal macrophages akin to those in DIP, **but** in a "bronchiolocentric" distribution (first- and second-order respiratory bronchioles). • Mild peribronchiolar fibrosis.	• As with DIP, presents with gradual onset of dyspnea and dry cough • symptoms recede with smoking cessation.

Done by: Leen Hajeer