RESPIRATORY PATHOLOGY SUMMARY

1- ASTHAM AND BRONCHIECTASIS:

- ASTHAMA: **type 1 hypersensitivity**

Initially: Allergens is recognized by ABC which induce TH2 cells to secrete:

IL-4+ IL-13 (mediates class switch to IgE)

IL-5 (activates eosinophils)

IL-13 (stimulates mucus production)

Re-exposure to allergen leads to IgE-mediated activation of mast cells:

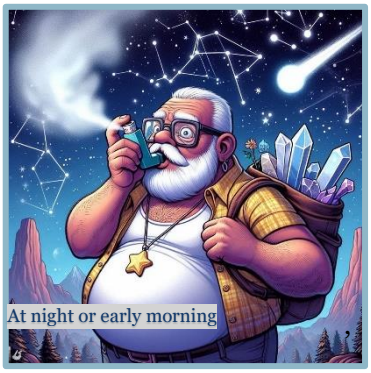
- Early-phase reaction: leukotrienes C4, D4, and E4 lead to bronchoconstriction mucus, and vasodilation, recruitment of leukocytes

- Late-phase reaction: Inflammation bc of production of chemokines from epithelial cells, especially protein derived from eosinophils=> damages epithelium

- Inflammation causes **airway remodeling**, involves:

bronchial smooth muscle and the **mucus glands** hypertrophy/ increase vascularity/ deposition of subepithelial **collagen**

MORPHOLOGY



mucous plugs contain whorls of shed epithelium called **Curschmann spirals.** (كرش مان)

Charcot-Leyden crystals: crystalloids made up of the eosinophil protein galectin-10

atopic	Non-atopic	DRUG-INDUCED	OCCUPATIONAL
most common • beginning in **childhood** • Positive family history • allergic rhinitis, urticaria, or eczema. •**Skin test / serum radioallergosorbent tests (RASTs):** determine the subject is allergic to.	• Negative skin test • A positive family history of asthma is less common. • Triggered by: • viral respiratory infections • inhaled air pollutants	Eg: Aspirin • rhinitis, nasal polyps, urticaria, and bronchospasm. • from inhibition of cyclooxygenase by aspirin	fumes, organic and chemical dusts, gases • Asthma attacks usually develop after repeated exposure to the antigen

status asthmaticus: Severe bronchospasm that does not respond to therapy, associated with hypercapnia, acidosis, and severe hypoxia in some patients it's fatal.

Therapies:• Anti-inflammatory (glucocorticoids) /Bronchodilators (beta-adrenergic drugs)/ Leukotriene inhibitors

- BRONCHIECTASIS:

• Permanent dilation X4 of bronchi and bronchioles (lower lobes **bilateral**)

• associated with **chronic necrotizing infections** /always occurs secondary to:

- **persistent infection**: Staphylococcus aureus or Klebsiella spp

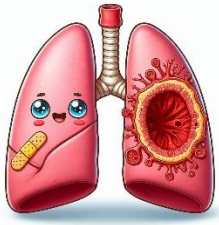
- **obstruction**: localized/ complication of atopic asthma and chronic bronchitis

- predisposed by **Congenital or hereditary conditions:**

• Cystic fibrosis

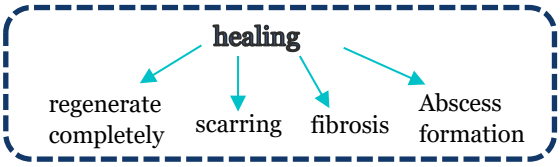
• Immunodeficiency states: localized or diffuse

• purulent sputum, sever cough, dyspnea, rhinosinusitis



• Primary ciliary dyskinesia (immotile cilia syndrome): AR/ bronchiectasis + sterility in males

-acute and chronic inflammatory exudate within the walls of the bronchi and bronchioles =>desquamation of lining epithelium and extensive ulceration



• cultured from the sputum •Diagnosis: histology+ radiology

• episodic => precipitated by URTI.

• Complications include hypoxemia with cor pulmonale and hypercapnia.

2- CHRONIC INTERSTITIAL (RESTRICTIVE, INFILTRATIVE) LUNG DISEASES, PART 1+2+3:

CHRONIC INTERSTITIAL LUNG DISEASES:

•inflammation and fibrosis of the lung interstitium (+/- intra-alveolar)

• Clinically: dyspnea, tachypnea, end-inspiratory crackles, and eventual cyanosis.

• **bilateral** lesions: small nodules, irregular lines, or ground-glass shadows/*patchy*.

• advanced: *diffuse* scarring "honeycomb"/ cor pulmonale. / Difficult to determine etiology

1- GRANULOMATOUS DISEASES:

A- SARCOIDOSIS: etiology is unknown.

•*Noncaseating epithelioid granuloma*: discrete outer CD4+ T cells with intermixed multinucleate giant cells.

-an outer zone rich in CD4+ T cells (**Trees**) with intermixed multinucleate **giant** cells.
-onion: Schaumann bodies
-star: Asteroid bodies
- road (SBEL سبيل): Skin, Spleen, BM, eye and lacrimal glands, Lungs, lymph nodes, Liver.

1- Schaumann bodies: hyalinized scars. (onion like)/2- Asteroid bodied

Lung 90%	LYMPH NODES (almost all)	SKIN 25%	EYE AND LACRIMAL GLANDS 25-50%
Granulomas: interstitium, +/- alveolar pleural. granulomas in submucosa BAL fluid => CD4+ T cells.	Painless, firm, rubbery • Discrete, nonadherent	Erythema nodosum: anterior legs. Subcutaneous nodules painless -septal panniculitis	**-UVEITITS** (MOST COMMON) uni or bi **-SICCA SYNDROME:** suppression of lacrimation. **-Mikulicz syndrome:** Combined uveoparotid involvement.
Spleen	Liver	Bone marrow	Hypercalcemia and hypercalciuria

-Mostly asymptomatic. **- steroids** -Diagnosis of exclusion.

B- HYPERSENSITIVITY PNEUMONITIS: (allergic alveolitis)/ prolonged exposure to inhaled organic antigens.

• CD4+ and CD8+ lymphocytes

•interstitial pneumonitis/ interstitial fibrosis with fibroblastic foci (in late stages).

•In advanced chronic cases UIP, **bilateral**, upper-lobe-dominant

• 2/3 of patients, Noncaseating granulomas ("Loose," peribronchiolar location)

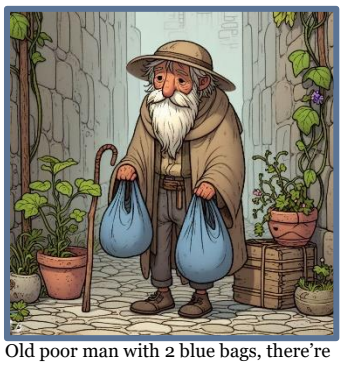
ACUTE REACTION: hrs after exposure (influenza like), exposure is terminated =>complete resolution /diagnosis is obvious.

CHRONIC PHASE: exposure in low dose for a long time results /insidious onset.

1. Farmer's lung
2. Humidifier or air-conditioner lung
3. Hot tub lung: nontuberculous Mycobacterium
4. Pigeon breeder's lung

2- FIBROSING DISEASES:

A- IDIOPATHIC PULMONARY FIBROSIS: cryptogenic Fibrosing alveolitis.



Old poor man with 2 blue bags, there're plants on Cobblestones.

•**bilateral** interstitial fibrosis, Lower lobe.

• (UIP)=> (**early and late lesions coexist**)

• Diagnosis of exclusion

•+/- Foci of squamous metaplasia and s.m hyperplasia

• Cobblestones appearance of the pleural surface

• "dry" or "Velcro"-like crackles during inspiration

•**believed to result from**: Repeated activation/injury (TGF-B)/ Genetic predisposition (surfactants, telomerase)/ Defective repair of alveolar epithelium

• Cyanosis, cor pulmonale, and peripheral edema.

•**old males**/The overall prognosis remains poor

•lung transplantation

• Anti-inflammatory therapies/Anti-fibrotic therapies

B- NONSPECIFIC INTERSTITIAL PNEUMONIA: Chronic bilateral interstitial fibrosis of Unknown etiology or associated with **collagen vascular disorders** such as rheumatoid arthritis.

Better prognosis/ female nonsmokers in their 6th decade

Key features: **bilateral**, symmetric, predominantly lower lobe reticular opacities.

lesions are of the same age.

divided into **cellular**: mild to moderate chronic interstitial inflammation. and **fibrosing patterns**: diffuse or patchy interstitial fibrotic lesions of the same stage of development.

C- CRYPTOGENICORGANIZINGPNEUMONIA:

Uncommon/Unknown etiology (graft-versus-host disease in BM transplant recipients).

• CXR: subpleural or peribronchial patchy airspace consolidation

• **Masson bodies:** loose organizing connective tissue (of the same age) in **air spaces.**

• Thus, the underlying lung architecture is normal.

• no interstitial fibrosis or honeycomb lung.

• oral **steroids.**

D-PNEUMOCONIOSIS: =>**may develop (PMF)** => cor pulmonale

ENTITY	EXPOSURE	PATHOLOGIC FINDINGS	COMMENTS
Coal Workers' Pneumoconiosis	Carbon dust; seen in coal miners	• **Asymptomatic anthracosis** (co_2 pigment) • **Simple coal worker's pneumoconiosis** (CWP): macrophages/ coal macules and nodules (respiratory bronchioles, upper lobe) • **Complicated CWP**: multiple, dark black scars dense collagen	• may also develop centrilobular emphysema and chronic bronchitis. • PMF tends to progress in the absence of further exposure.
Silicosis  Cloud for upper	Silica; seen in silica miners	•Two types: crystalline silica (toxic) and amorphous • Silicotic nodules: arranged hyalinized collagen fibers surrounding amorphous center. • Polarized microscopy reveals weakly birefringent silica(crystals) • in **upper zone** of the lung	• Increased risk for TB/ x2 lung cancer risk. • Most X shortness of breath until late in the course. • When mixed with other minerals, the fibrogenic effect of quartz is reduced.

Asbestosis 	ASBESTOS FIBERS EXPOSURE	• Diffuse pulmonary interstitial fibrosis indistinguishable from UIP. • Asbestos bodies: golden brown, formed of asbestos fibers coated with an iron • Begins in the lower lobes and subpleurally (spreading at fibrosis progresses) • Pleural plaques: M.C	•risk for mesothelioma is 1000 times greater than the lung cancer • Asbestos exposure →x5 lung carcinoma • Asbestos exposure and smoking together →x55 lung carcinoma

3- PULMONARYEOSINOPHILIA:

-immunologic origin, characterized by pulmonary infiltrates rich in eosinophils

4- SMOKING-RELATEDINTERSTITIAL DISEASES:

- Both may cause emphysema/ gradual onset/ Presence of pigmented macrophages

A- DESQUAMATIVE INTERSTITIAL PNEUMONIA (DIP): in the alveolar air spaces

• excellent response to steroids and smoking cessation • good prognosis

B- RESPIRATORY BRONCHIOLITIS- ASSOCIATED INTERSTITIAL LUNG DISEASE:

•Aggregates of smokers' macrophages within: Respiratory bronchioles, alveolar ducts, and peribronchiolar spaces

• Cessation of smoking usually results in improvement.

3- PULMONARY DISEASES OF VASCULAR ORIGIN:

A- PULMONARY EMBOLISM, HEMORRHAGE, AND INFARCTION:

1- THROMBOEMBOLISM:

large deep veins of the legs, most often popliteal vein

CONSEQUENCES: • Ischemia

• Increase in pulmonary artery pressure and vasospasm thromboxane A2, and serotonin)

MORPHOLOGY:

1-No morphologic alternations: large emboli (causing sudden death)

2-Alveolar hemorrhage occurs in: smaller emboli 3-Infarction: not common

MANAGEMENT: Prophylactic therapy/Anti-coagulation / Thrombolytic therapy

• Occurs with compromised cardiovascular status (congestive heart failure)

• more peripheral the embolic occlusion= higher the risk

lower lobes & >50% are multiple infarcts.

• wedge-shaped, base at the pleural surface and the apex toward the hilus

2- NONTHROMBOTIC PULMONARY EMBOLI:

Uncommon but potentially lethal/Bone marrow embolism: bone infarction secondary to sickle cell anemia.

• PULMONARY HYPERTENSION: 25 mm Hg or more at rest

Pulmonary arterial hypertension: Heritable	Pulmonary hypertension due to left-sided heart disease	Pulmonary hypertension due to lung diseases and/or hypoxia	Chronic thromboembolic pulmonary hypertension	Pulmonary hypertension with unclear or multifactorial mechanisms

•Morphology: Medial hypertrophy (large vessels) +Medial hypertrophy and intimal fibrosis (small arteries)+ Right ventricular hypertrophy+ Plexiform lesions 1&2

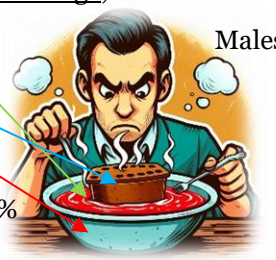
• DIFFUSE ALVEOLAR HEMORRHAGE SYNDROMES:

1. GOODPASTURE SYNDROME:

• begin with hemoptysis

• lung and kidney(glomerulonephritis) injury are caused by circulating autoantibodies against IV collagen

•MICROSCOPICALLY: Focal necrosis of alveolar wall with intra-alveolar hemorrhage, Fibrous thickening of septa, Hypertrophic type II pneumocytes, Abundant hemosiderin



Males>

•Plasmapheresis and immunosuppressive /Renal transplantation

2. IDIOPATHIC PULMONARY HEMOSIDEROSIS

3. GRANULOMATOSIS WITH POLYANGIITIS: PR3-ANCAs in 95%

•Triad of:

1) Necrotizing angiitis

2) Aseptic necrosis of the upper & lower respiratory tract

• poorly formed granulomatous inflammation

3) Focal glomerulonephritis

•PR3-ANCAs in 95%

4- LUNG CANCER 1+2:

CANCER	CHARACTERISTIC	MORPHOLGY	LOCATION	COMMENT
Adenocarcinoma	acinar (gland-forming)/ mucus production	-**Atypical adenomatous hyperplasia** (AAH): small precursor lesion lining alveolar walls - **adenocarcinoma in situ (AIS):** dysplastic cells growing along pre-existing alveolar septa -**Adenocarcinoma, m.invasive or invasive**	Peripheral	• tend to metastasize widely at an early stage Most common tumor in nonsmokers
squamous cell carcinomas 	• Well differentiated squamous cell neoplasms showing keratin pearls and intercellular bridges	• **squamous metaplasia or dysplasia** in the bronchial epithelium **➔carcinoma in situ ➔ Squamous cell carcinoma** (invasive)	Central	• More common in smoker men - Centrally in major bronchi =>spread to local hilar nodes • Large lesions => central **necrosis**=>cavitation.
small cell lung carcinoma 	By the time of diagnosis, most will have metastasized to hilar and mediastinal lymph nodes.	Small tumor cells (salt and pepper appearance) • Frequent mitotic figures • Necrosis invariably present • Express neuroendocrine markers "Crush artifact"/ Nuclear molding	centrally located or peripherally located	metastasizing widely - smokers - Azzopardi effect: basophilic staining of vascular walls due to accumulation of the DNA of necrotic tumor cells -poor prognosis
Large cell carcinoma		• Large irregular nuclei, prominent nucleoli, and a moderate amount of cytoplasm and atypia.		• Are undifferentiated malignant epithelial tumors.
Carcinoid tumor	-neuroendocrine -2 patterns: Polypoid/a mucosal (collar-button lesion)	• Typical carcinoids nests of uniform cells "salt-and-pepper" chromatin, rare mitoses • Atypical carcinoid: higher mitotic and small foci of necrosis. /Lymph node and distant metastasis than/TP53	Central or peripheral (less common)	• May occur as part of the multiple endocrine neoplasia syndrome (MEN syndrome) Rarely => carcinoid syndrome: attacks of diarrhea, flushing, abdominal pain, and cyanosis.
Malignant mesothelioma	Preceded by extensive pleural fibrosis and plaque	• Have one of three: (1) Epithelial: cuboidal cells (2) sarcomatous: spindled cells grow in sheets (3) biphasic: both sarcomatous and epithelial areas		Begin in a localized area and spread widely.

• Left supraclavicular node (Virchow node) involvement is particularly characteristic.

• Pancoast tumors (Pancoast syndrome): Invade the brachial or cervical sympathetic plexus

• Hoarseness of voice, chest pain, superior vena cava syndrome, pericardial or pleural effusion, or persistent segmental atelectasis or pneumonitis

• Symptoms from metastatic spread: Brain / Liver / Bones

PARANEOPLASTIC SYNDROMES:

(1) Hypercalcemia (PTH): SCC

(2) Cushing syndrome (ACTH): SCLC, CARCINOID

(3) Syndrome of inappropriate secretion of ADH, hyponatremia: SCLC

(4) Acromegaly (GHRH) or (GH): SCLC, CARCINOID

(5) Neuromuscular syndromes

(6) hypertrophic pulmonary osteoarthropathy (finger clubbing) Adenocarcinoma, SCC

(7) Coagulation abnormalities

5- TUBERCULOSIS:

TUBERCULIN (MANTOUX) TEST: intracutaneous injection of 0.1 mL of (PPD)=> A positive tuberculin skin test does not differentiate between infection and disease.

unexposed immunocompetent: Development of cell-mediated immunity/Destructive tissue hypersensitivity ■ Caseating granulomas ■ Tissue destruction and Cavitation ■ immunity to the organism.

-entry is mediated by many receptors expressed on **surface of macrophages** like mannose=>inhibit the normal microbicidal by **inhibiting fusion of phagocytic vacuole that they are inside and lysosome**=>ABC recognize it and release **IL 12 that activates type 1 T helper** lymphocyte=> type 1 T helper lymphocyte releases interferon gamma =>activation of macrophages into epithelioid macrophages or **"epithelioid histiocytes"** release TNF and chemokines=>**granulomas**

-**Reactivation or re-exposure** =>results in rapid mobilization of a defensive reaction but also increased tissue necrosis

■ ***MILIARY PULMONARY DISEASE:***

When organisms reach the bloodstream through lymphatic vessels and then recirculate to the lung via the pulmonary arteries. (yellow-white consolidation scattered through the lung parenchyma)

■ ***SYSTEMIC MILIARY TUBERCULOSIS***

■Lymphadenitis the most frequent form of extrapulmonary tuberculosis/ cervical region.

-Conventional cultures (10 weeks)

Primary Tuberculosis:	*Secondary Tuberculosis*
close to the pleura in the distal air spaces	apex of one or both upper lobes
– in the lower part of the upper lobe	-central caseation and peripheral fibrosis
– in the upper part of the lower lobe.	-**tubercle bacilli**: in early exudative and caseous phases of granuloma formation/Impossible in the late fibrocalcific stages.
■ **Ghon focus**: central caseous necrosis.	–Erosion into a bronchus => irregular cavity lined by caseous material/Erosion of blood vessels results in hemoptysis.
■ **Ghon complex**: This combination of parenchymal and nodal lesions	

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